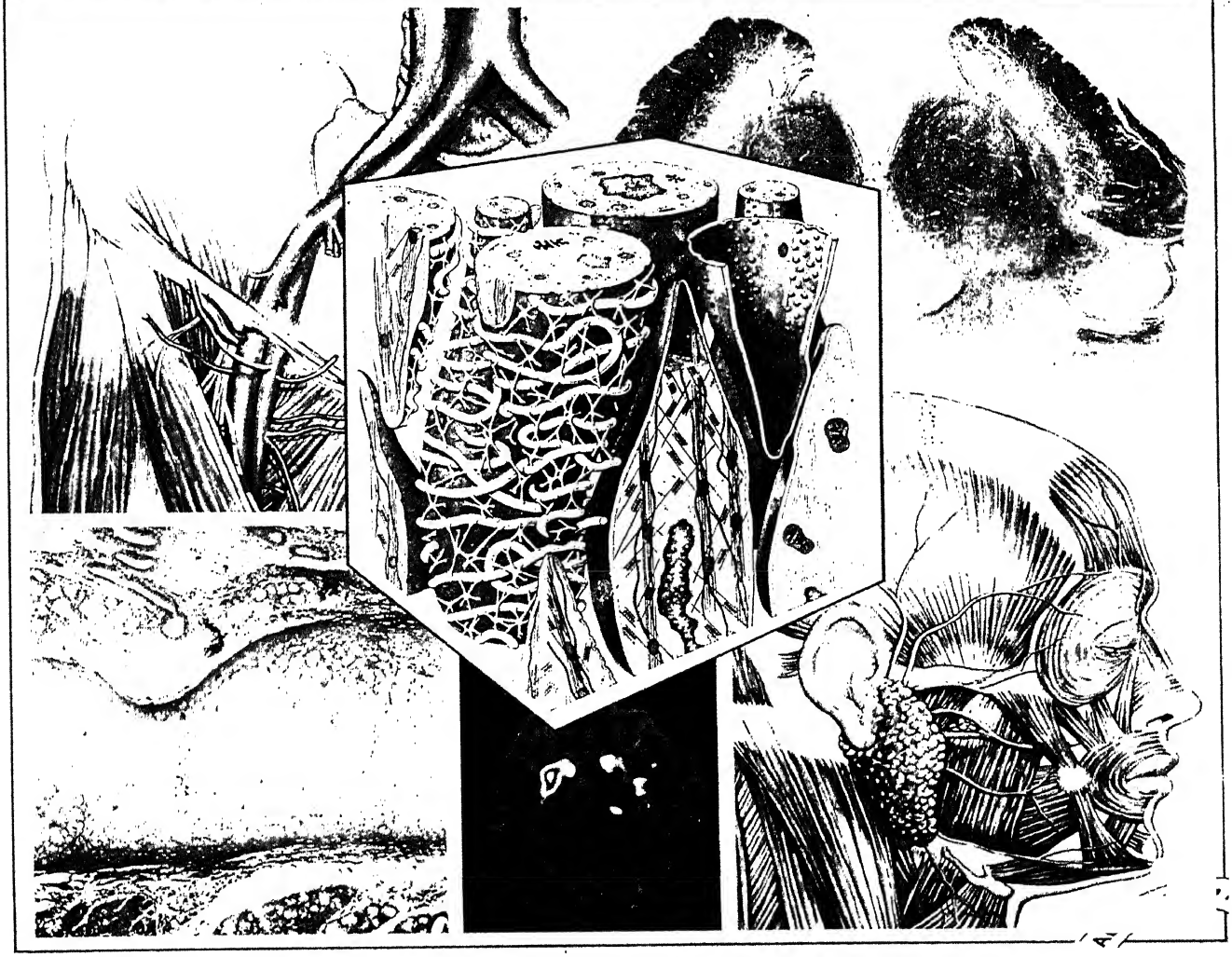
THIRTY-EIGHTH EDITION

GRAY'S ANATOMY



CHURCHILL LIVINGSTONE

GRAY"S ANATOMY

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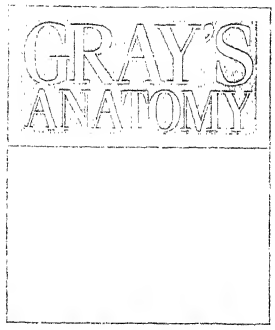


NEONATAL ANATOMY AND GROWTH

Section Editor: Patricia Collins

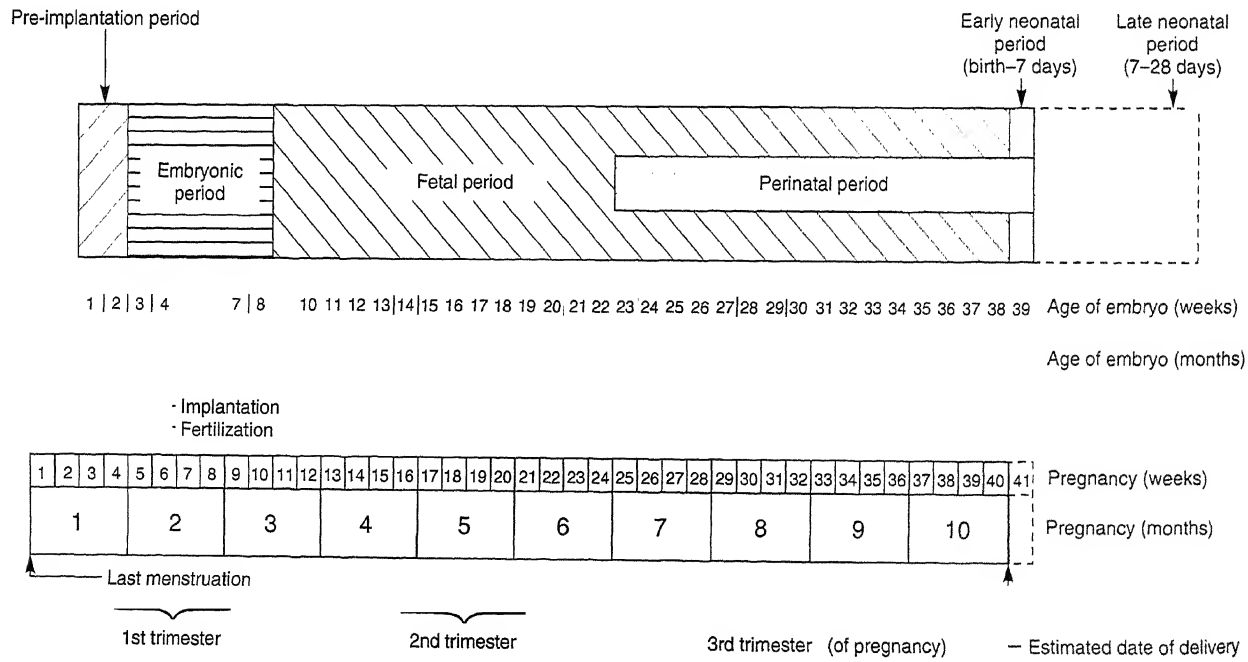
Professor Edmund Crelin's publications provided much of the data for this chapter. The late Professor Peter Williams nurtured the inspiration, encouraged the development and supported the final birth of the chapter. Vitality has been added by two artists, Peter Jack and Peter Lamb; and Dr Mike Hall supplemented the whole with an essay on neonatal procedures. I am grateful to them all.

Neonatology as a distinct discipline has a fairly recent origin. In Western societies technological advances have enabled successful management of full-term neonates to form the basis of care for preterm infants, many at ages which were considered non-viable a decade or two previously. Now, the study of neonatology very much overlaps the later stages of embryology and development. Preterm infants, although obviously past organogenetic processes, are still engaged in maturational processes with local interactions and pattern formation driving development at local and body system levels. The sudden release of such fetuses into a gaseous environment, of variable temperature, with full gravity and a range of micro-organisms, promotes the rapid maturation of some systems and the compensational growth, in terms of effect of gravity, or enteral feeding, or exposure to micro-organisms, of others. To understand this multitude of mechanisms operating within a newly delivered fetus, as much information concerning normal embryological and fetal development as possible is required. Today there are many texts on neonatal physiology but fewer which set out the basic differences between the anatomy of the full-term neonate and the adult. However, just as there are immense differences in the relations of some structures between the full-term neonate, child and adult, so there are also major differences between the 20 week gestation fetus and the 40 week fetus, just prior to birth. Thus the study of fetal anatomy at 20, 25, 30 and 35 weeks is vital for the investigative and life-saving procedures carried out on preterm infants today. This section has drawn together the available information on the anatomy of the full-term (40 week gestation, see below) neonate and added, where appropriate, notes on the preterm neonate. The reader is recommended to consult Crelin (1973) from which much of the basic anatomical information was acquired. Crelin notes particularly that the newborn infant is not a miniature adult; it is also important to note that very low-weight, early preterm, infants are similarly not the same as full-term infants.

Estimation of the developmental age of neonates

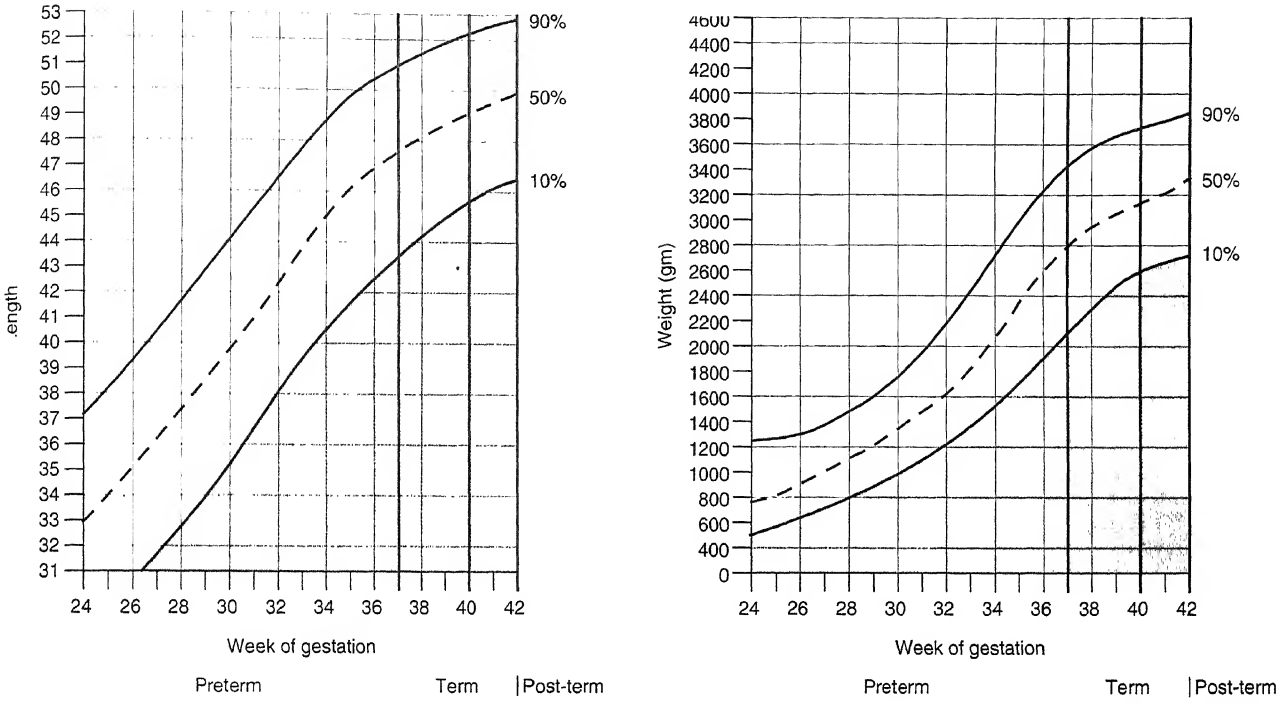
The development of embryos is described in terms of 'stages' (see p. 135), each stage being a time period during which a variety of systems or organs attain a particular stage of development. Such embryonic stages are based on a linear scale of development commencing at fertilization and ending at stage 23 (8 weeks after fertilization) when the embryo becomes a fetus. Using this scale, development averages 266 days, or 9.5 months. To estimate the **length of a pregnancy** to provide an estimated date of delivery, the commencement of gestation is traditionally determined **clinically** by counting from the date of the last menstrual period. Estimated in this manner it averages 280 days, or 10 lunar months (40 weeks). 4.1 shows the two time scales used to depict embryonic development and the stage of pregnancy. Throughout the Embryology section, development is described from the time of fertilization, as depicted in the upper scale in 4.1. However, when discussing fetal development and the gestational age of neonates, particularly those born before 40 weeks gestation (see below), the clinically estimated stage is invariably used in the literature. Thus in Neonatology and Growth descriptions of fetal stages and neonatal anatomy are related to the lower of the scales in 4.1, the clinically derived weeks of pregnancy.

The period of pregnancy is often divided into thirds, termed *trimesters*. The first and second trimesters each cover a period of 12 weeks, and the third trimester covers the period from 24 weeks to delivery. Although the expected date of delivery is computed at 40 weeks of pregnancy, the *term* of the pregnancy, i.e. its completion resulting in delivery, is considered normal between 37 and 42 weeks. Neonates delivered before 37 weeks are called *preterm* (or *premature*) and after 42 weeks, *post term*. The period immediately prior to, and up to 7 days after, birth is termed the *perinatal period*; the commencement of the perinatal period is from the end of week 24 and infants born from this stage of pregnancy are classed as stillborn and contribute to the statistics of perinatal mortality if they die, whereas those fetuses which are delivered and die prior to this time are considered to be miscarriages of pregnancy. The technological advances in neonatal care can now assist the delivery and support of infants younger than 24 weeks. The *neonatal period* extends from birth to 28 days postnatally; it is divided into an early neonatal



4.1 The two times scales used to depict human development. Embryonic development, in the upper scale, is counted from fertilization (or from ovulation, i.e. in postovulatory days; see O'Rahilly & Muller 1987). Times given for development in the Embryology and Development section are based on this scale. The clinical estimation of pregnancy is counted from the last menstrual period and is shown on the lower scale. Fetal ages given in the Neonatal Anatomy and Growth section will have been derived from the lower scale. Note that there is a two-week discrepancy between these scales. The perinatal period is very long as it includes all of the preterm deliveries.

STANDARD CHARTS OF PRENATAL GROWTH



4.2 Standardized graphs of fetal length (A) and weight (B) from 24 weeks of pregnancy showing the 10th, 50th and 90th centiles.

period from birth to 7 days, and a late neonatal period from 7 to 28 days.

Neonatal measurements and gestational age

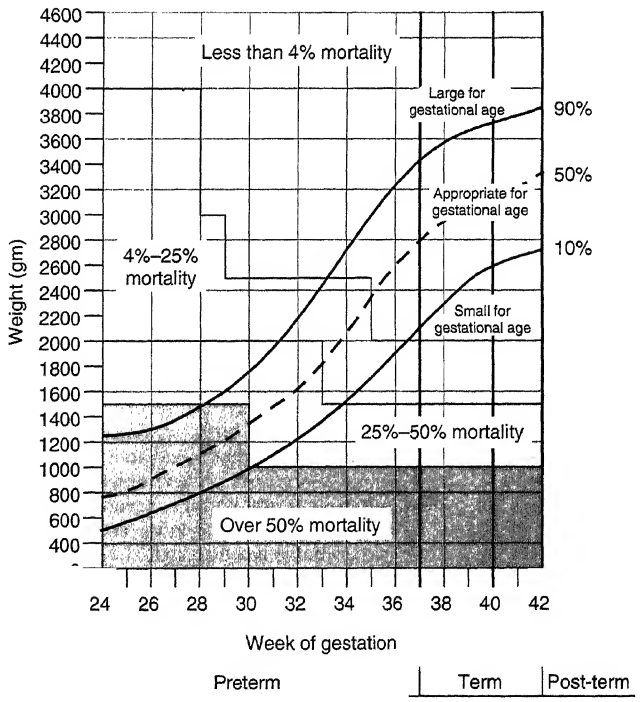
The **length** of the full-term neonate ranges from 48 to 53 cm (4.2A). Length of the newborn is measured from crown to heel (CHL); however, in utero length is estimated from crown–rump length (CRL), i.e. the greatest distance between the vertex of the skull and the ischial tuberosities, with the fetus in the natural curved position. Crown rump length is very reliable for estimating gestational age between weeks 7 and 14. The **weight** of the full-term infant at parturition ranges from 2700–4000 g (4.2B), the average being 3400 g; 75–80% of this weight is body water with a further 15–28% composed of adipose tissue. After birth there is a general decrease in the total body water but a relative increase in intracellular fluid. Normally the newborn loses about 10% of the birth weight by 3–4 days postnatally because of loss of excess extracellular fluid and meconium. By 1 year total body water makes up 60% of the body weight.

Two populations of neonates are at particular risk:

- those with known low gestational dates, i.e. *preterm infants* (see above)
- those with a low birth weight.

Low birth weight has been defined as under 2500 g, with *very low birth weight* being under 1500 g. Infants may weigh less than 2500 g but not be premature by gestational age. Collection of the range of weights fetuses may attain before birth has led to the production of weight charts which allow babies to be described according to how appropriate their birth weight is for their gestational age, for example small for gestational age (SGA), appropriate for gestational age (AGA), and large for gestational age (LGA) (4.3). Small for gestational age infants are often the result of *intrauterine growth retardation (IUGR)*; the causes of growth retardation are many and various and beyond the scope of this text.

For both premature infants and growth retarded infants an assessment of gestational age, which correlates closely with the stage of



4.3 Graph showing intrauterine growth status and its appropriateness for gestational age. Gestational age is more closely related to maturity than birth weight. The mortality for the weight ranges is indicated.

maturity, is desirable. Gestational age at birth is predicted by its proximity to the estimated date of delivery and the results of the ultrasonographic examinations during pregnancy (see p. 340). It is currently assessed in the neonate by evaluation of a number of external physical and neuromuscular signs. Scoring of these signs results in a cumulative score of maturity which is usually between ±2 weeks of the infant's true age. The scoring scheme has been devised and improved over many years from gestational age assessments proposed by, inter alia, Robinson (1966), Farr et al (1966), Dubowitz et al (1970) and Dubowitz and Dubowitz (1981). For a recent account of these methods of assessing gestational age consult Gandy (1992).

GASTROINTESTINAL SYSTEM

Oral cavity. This cavity is only potential with the mouth closed. The tongue is short and broad, and its entire surface lies within the oral cavity (4.4). The posterior third of the tongue descends into the neck during the first postnatal year and by the fourth or fifth year the tongue forms part of the anterior wall of the pharynx. The hard palate is only slightly arched; it is usually corrugated by five or six irregular transverse folds which assist the newborn when suckling. The epiglottis is high and makes direct contact with the soft palate. During suckling three spaces are formed in the oral cavity. A median space between the tongue and hard palate divides into two posteriorly, forming channels each side of the approximated soft palate and epiglottis. Two lateral spaces, *lateral arcuate cavities*, are formed between the tongue medially and the cheeks laterally; the upper and lower gums situated in these spaces do not touch during suckling. Each cheek is supported by a mass of subcutaneous fat which lies between the buccinator and masseter muscles; it is sometimes termed the *suctorial pad*. As fluid passes from the oral spaces to the pharynx, the larynx is elevated so that its opening is **above** the level of the spaces which convey fluid to the pharynx. The high position of the larynx and its further elevation during suckling directs its opening into the nasopharynx enabling babies to breath while suckling. It was thought for many years that neonates preferentially breathe through the nose, resorting to mouth breathing only if the nasal passage is obstructed. Studies have shown that full-term infants are able to establish oral breathing in the presence of nasal occlusion of a mean duration of 7.8 seconds (Rodenstein 1985).

Salivary glands. These glands have the same relative weight in the neonate as in the adult. The topography of the submandibular and sublingual glands is the same as in the adult, whereas the parotid gland is rounded, lying between masseter and the ear. With growth, during infancy and early childhood, the parotid gland covers the parotid duct.

Pharynx. In the neonate this is one-third of the relative length in the adult. The nasopharynx is a narrow tube which curves gradually to join the oropharynx without any sharp junctional demarcation. An oblique angle is formed at this junction by 5 years of age and in the adult the nasopharynx and oropharynx join at almost a right angle.

Hyoid bone. In a relatively higher and more anterior position in the neonate (4.4), it has a small ossification centre in the body of the bone, which is mainly cartilaginous at birth. Its two constituent parts, derived from the second and third pharyngeal arch cartilages, can be identified from the horizontal groove present along the body. The length of the hyoid bone from greater cornu to greater cornu is 3 cm. The stylohyoid ligament attached to the lesser cornu of the hyoid passes to a more horizontally inclined styloid process. In infancy the hyoid bone descends with the larynx to a lower position in the neck.

Larynx. About one-third the size of the adult, although it is proportionately larger in the neonate, its cavity is short and funnel-shaped. At rest the upper border of the epiglottis is at the level of the second or third cervical vertebra; when the larynx is elevated it is at the level of the first cervical vertebra. The *thyroid cartilage*, which is shorter and broader than the adult, lies closer to the hyoid bone in the neonate. Neither the superior notch nor the laryngeal prominence is as marked as in the adult. The *cricoid cartilage* is the same shape as in the adult. The *vocal folds* are 4–4.5 mm long, relatively shorter than in childhood and the adult. The ventricle of the larynx is small; however, the saccule of the larynx is often considerably larger. Unlike the adult, the neonatal subglottic cavity extends posteriorly as well as inferiorly, an important fact to be considered when passing an endotracheal tube. The mucosa of the larynx readily becomes oedematous after irritation, in the neonate and infant, which may lead to obstruction of the airway.

By about the third year sexual differences are apparent in the larynx; it becomes larger in boys and the angle between the thyroid laminae is more pronounced in girls. At puberty these changes increase, with greater enlargement of the male larynx. The angle of union of the thyroid laminae is about 120° in women and 90° in men.

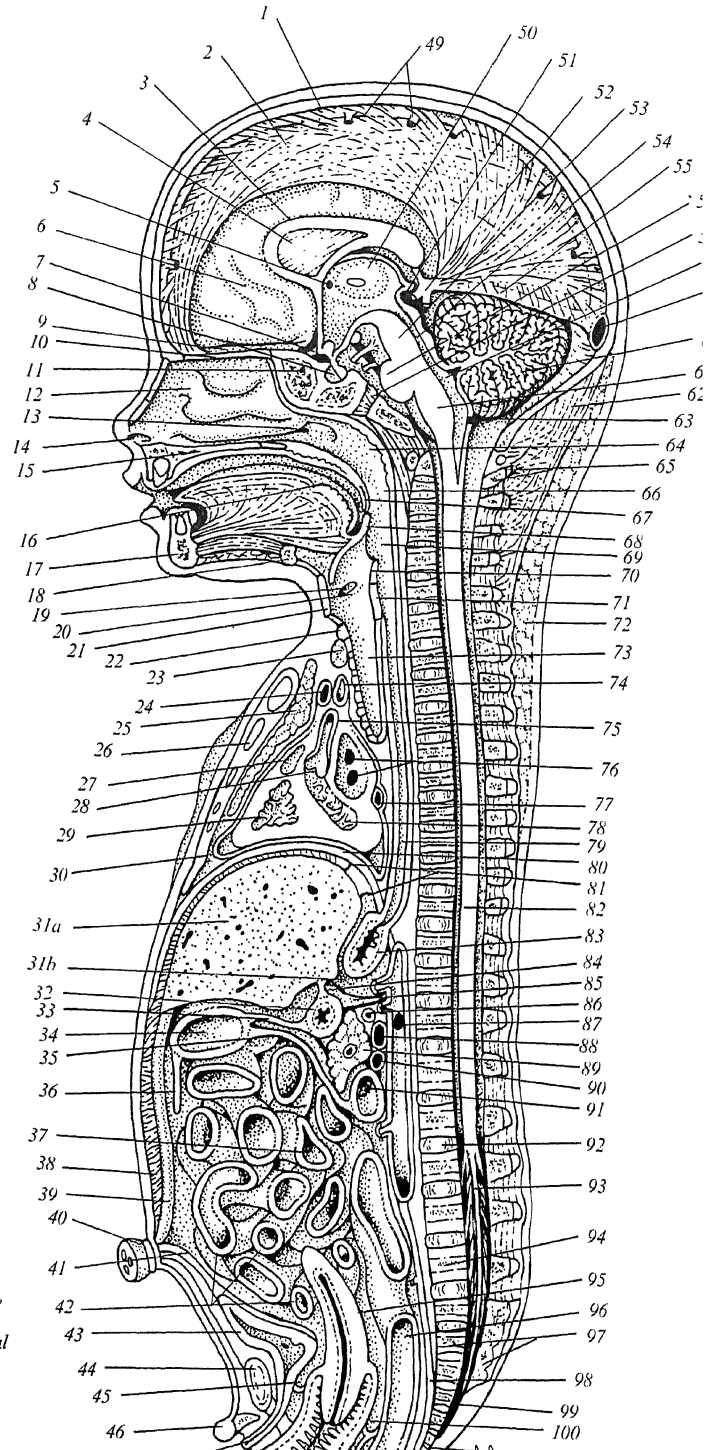
Oesophagus. At birth this extends 8–10 cm from the cricoid cartilage to the gastric cardiac orifice. It commences and ends 1–2 vertebrae higher than in the adult, extending from between the fourth to the sixth cervical vertebrae to the level of the ninth thoracic vertebra. Its average diameter is 5 mm and it possesses the constrictions seen in the adult. The narrowest constriction is at its junction with the pharynx, where the inferior pharyngeal constrictor muscle functions to constrict the lumen; it is this region which may be easily traumatized with instruments or catheters. In the neonate the mucosa may contain scattered areas of ciliated columnar epithelium; these disappear soon after birth.

Stomach. This exhibits fetal characteristics until just after birth when the initiation of pulmonary ventilation, the reflexes of coughing and swallowing, and crying, cause the ingestion of large amounts of air and liquid. Once postnatal swallowing has commenced the stomach distends to four or five times its contracted state and shifts its position in relation to the state of expansion and contraction of the other abdominal viscera, and to the position of the body. Generally, in the neonate, the anterior surface of the stomach is covered by the left lobe of the liver which extends across nearly as far as the spleen (4.5, 6). Only a small portion of the greater curvature of the stomach is visible anteriorly. The capacity of the stomach is between 30–35 ml in the full-term neonate, rising to 75 ml in the second week and 100 ml by the fourth week (adult capacity is on average 1000 ml). The mucosa and submucosa are relatively thicker than in the adult; however, the muscularis is only moderately developed without co-ordinated peristalsis. At birth gastric acid secretion is low, resulting in a high gastric pH for the first 12 postnatal hours. The pH then falls rapidly with the onset of gastric acid secretion, usually after the first feed. Generally acid secretion remains low for the first 10 days postnatally. Gastric emptying and transit times are delayed in the neonate (Nagourney & Aranda 1992).

Small intestine. This forms an oval-shaped mass with a greater diameter transversely orientated in the abdomen rather than vertically as in the adult (4.6). The mass of the small intestine inferior to the umbilicus is compressed by the urinary bladder which is anterior at this point (see below). The small intestine is 300–350 cm long at birth and its width when empty is 1–1.5 cm. The ratio between the length of the small and large intestine at birth is similar to the adult. The mucosa and submucosa are fairly well developed with villi throughout the small intestine (villi are present in the large intestine earlier in development, see p. 191); however, the muscularis is very thin, particularly the longitudinal layer, and there is little elastic tissue in the wall. Generally there are few or no circular folds in the small intestine, and the jejunum and ileum have little fat in their mesentery.

Large intestine. At birth this is about 66 cm long and averages 1 cm in width. The caecum is relatively smaller than in the adult; it tapers into the vermiform appendix. The ascending colon is shorter in the neonate, due to the shorter lumbar region; the transverse colon is relatively long; the descending colon is short, but twice the length of the ascending colon (4.5). The sigmoid colon may be as long as the transverse colon; it often touches the inferior part of the anterior body wall on the left and, in approximately 50% of neonates, part of the sigmoid colon lies in the right iliac fossa. Generally in the colon the muscularis, including the taeniae coli, is poorly developed as in the small intestine. Appendices epiploicae and haustra are not present, giving a smooth external appearance to the colon. Haustra appear within the first 6 months. The rectum is relatively

1. *Superior sagittal sinus*
2. *Falx cerebri*
3. *Corpus callosum*
4. *Septum pellucidum*
5. *Right interventricular foramen*
6. *Frontal lobe of right cerebral hemisphere*
7. *Optic nerve*
8. *Hypophysis*
9. *Olfactory nerve*
10. *Cribriform lamina*
11. *Sphenoid bone*
12. *Nasal cavity*
13. *Ostium of auditory tube*
14. *Naris*
15. *Hard palate*
16. *Foramen caecum of tongue*
17. *Mandible*
18. *Hyoid bone*
19. *Laryngeal ventricle*
20. *Vocal fold*
21. *Thyroid cartilage*
22. *Cricoid cartilage arch*
23. *Isthmus of thyroid gland*
24. *Left brachiocephalic vein*
25. *Thymus gland*
26. *Sternum*
27. *Auricle of right atrium*
28. *Aortic semilunar valves*
29. *Right ventricle*
30. *Pericardium*
31. *Liver*
    a. *left lobe*
    b. *caudate lobe*
32. *Pylorus of stomach*
33. *Gastrocolic ligament*
34. *Transverse colon*
35. *Transverse mesocolon*
36. *Greater omentum (apron)*
37. *Jejunum*
38. *Falciform ligament*
39. *Umbilical vein*
40. *Stump of umbilical cord*
41. *Median umbilical ligament*
42. *Ileum*
43. *Urinary bladder*
44. *Pubic symphysis*
45. *Vesico-uterine pouch*
46. *Clitoris*
47. *Urethra*
48. *Vagina*
49. *Superior cerebral veins*
50. *Thalamus protruding into 3rd ventricle*
51. *Pineal body*
52. *Great cerebral vein*
53. *Cerebral peduncle*
54. *Cerebral aqueduct*
55. *Straight sinus*
56. *Pons*
57. *Spheno-occipital synchondrosis*
58. *4th ventricle*
59. *Confluence of sinuses*
60. *Cerebellum*
61. *Medulla oblongata*
62. *Ligamentum nuchae*
63. *Median aperture of 4th ventricle*
64. *Nasal part of pharynx*
65. *Lamina and spinous process of 2nd cervical vertebra*
66. *Oral part of pharynx*
67. *Soft palate*
68. *Epiglottis*
69. *Laryngeal part of pharynx*
70. *Arytenoid cartilage*
71. *Cricoid cartilage lamina*
72. *Subcutaneous adipose tissue (interscapular brown fat)*
73. *Trachea*
74. *Brachiocephalic trunk*
75. *Ascending aorta*
76. *Openings of right pulmonary veins in left atrium*
77. *Coronary sinus*
78. *Left ventricle*
79. *Oesophagus*
80. *Diaphragm*
81. *Coronary ligament*
82. *Spinal cord*
83. *Cardiac part of stomach*
84. *Lesser omentum*
85. *Omental bursa*
86. *Splenic artery*
87. *Opening of right renal artery in aorta*
88. *Left renal vein*
89. *Pancreas*
90. *Splenic vein*
91. *Duodenum*
92. *Nucleus pulposus of intervertebral disc between 2nd and 3rd lumbar vertebrae*
93. *Filum terminale among spinal nerve roots (cauda equina) within vertebral canal*
94. *Body of 5th lumbar vertebra*
95. *Uterus*
96. *Rectum*
97. *Sacrum*
98. *Median sacral artery*
99. *Sacral hiatus*
100. *Recto-uterine pouch*
101. *Coccyx*
102. *Rectovaginal septum*
103. *Anal canal*
104. *Anococcygeal ligament*

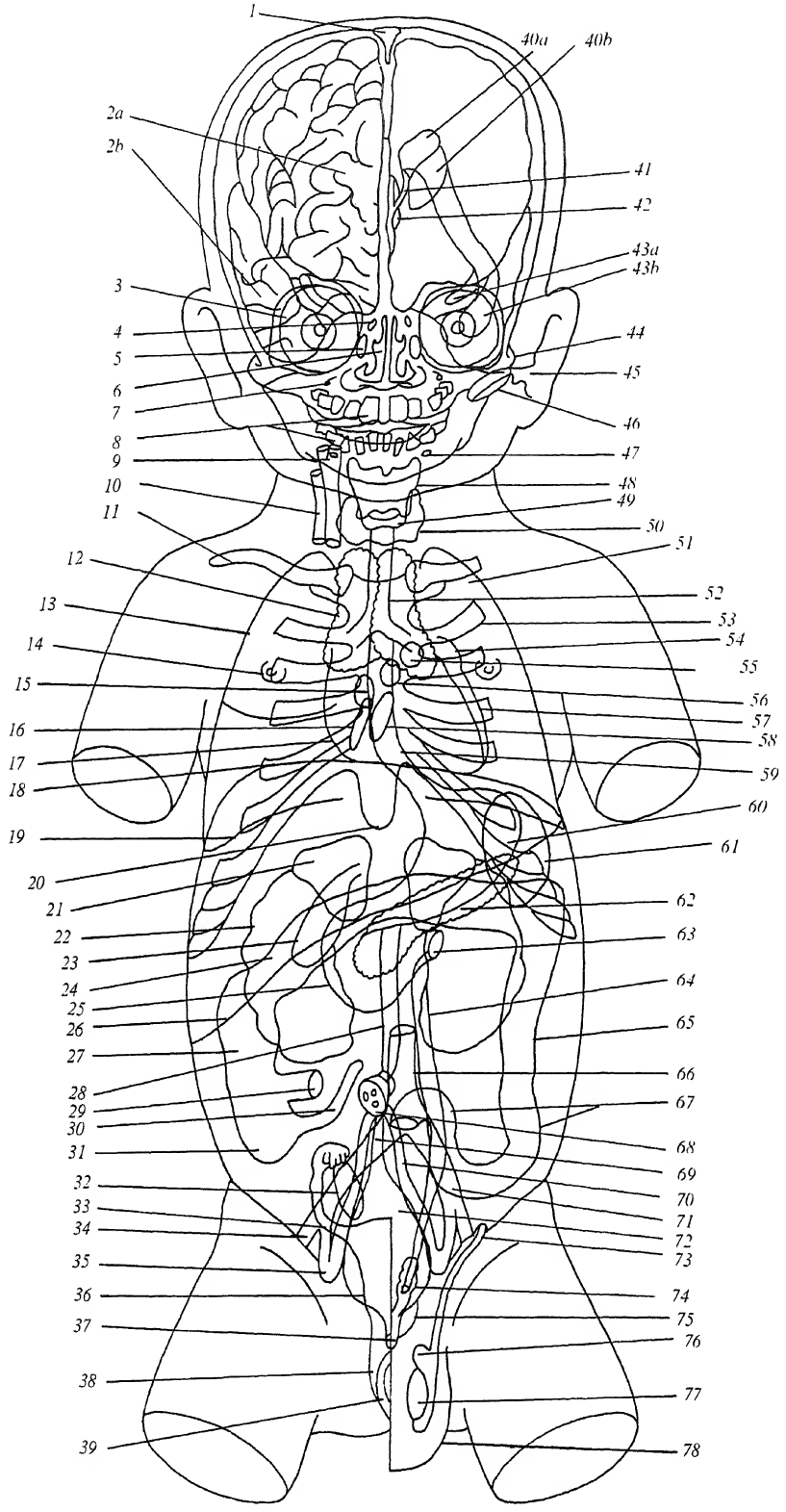


4.4 Midsagittal section through a full-term female neonate (after Crelin, Functional Anatomy of the Newborn).

long; its junction with the anal canal forms at nearly a right angle.

Meconium. This is a dark, sticky, viscid substance formed from the passage of amniotic fluid, sloughed cells, digestive enzymes and bile salts along the fetal gut. Meconium becomes increasingly solid as gestation advances but does not usually pass out of the fetal body while in utero. Fetal distress produced by anoxia may induce the premature defecation of meconium into the amniotic fluid, causing risk of its inhalation. At birth the colon contains 60–200 g of meconium. The majority of neonates defecate within the first 24 hours after birth.

Liver. This constitutes 4% of the body weight in neonates, compared to 2.5–3.5% in adults. It is in contact with the greater part of

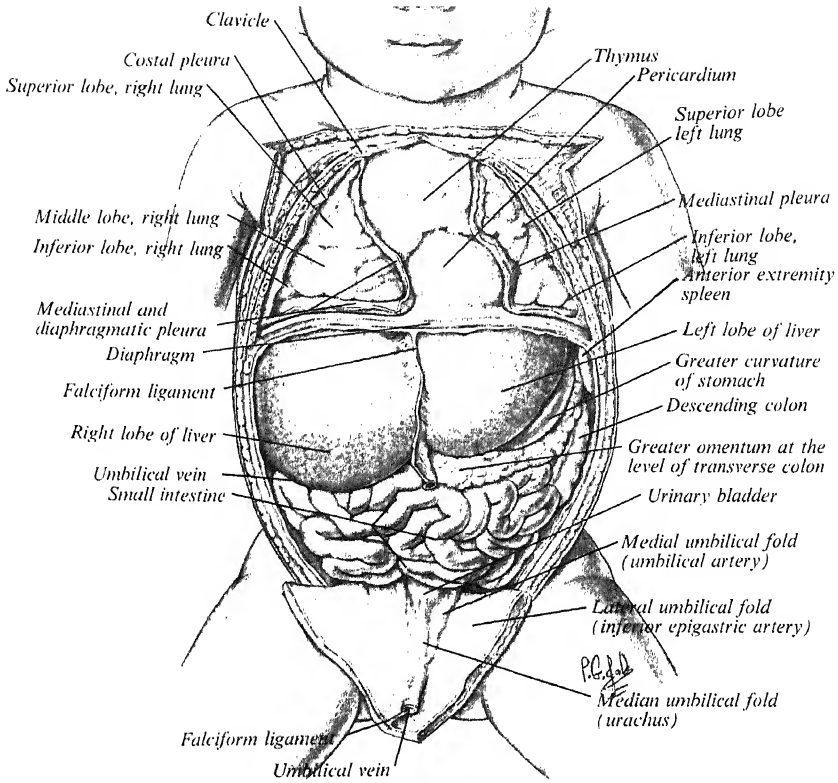


1. *Superior sagittal dural sinus*
2. *Right cerebral hemisphere*
   a. frontal lobe
   b. temporal lobe
3. *Eyeball*
4. *Ethmoid air cell*
5. *Maxillary sinus*
6. *Nasal cavity*
7. *Infraorbital foramen*
8. *Enamel of deciduous teeth*
9. *Bifurcation of common carotid artery*
10. *Internal jugular vein*
11. *Clavicle*
12. *Thymus gland*
13. *Right lung*
14. *Mammary gland areola*
15. *Foramen ovale*
16. *Right atrioventricular valve*
17. *Right border of heart*
18. *Superior border of liver and central level of diaphragm*
19. *Posterior inferior level of lung*
20. *Xiphoid process*
21. *Right suprarenal gland*
22. *Right kidney*
23. *Gallbladder*
24. *Transverse colon*
25. *Duodenum*
26. *Anterior inferior border of liver*
27. *Ascending colon*
28. *Umbilical vein*
29. *Ileum*
30. *Appendix*
31. *Caecum*
32. *Right ovary*
33. *Uterine tube*
34. *External iliac artery*
35. *Right umbilical artery*
36. *Right half of uterus*
37. *Urethra*
38. *Vagina*
39. *Hymen*
40. *Left lateral ventricle*
    a. central part
    b. anterior horn
41. *Interventricular canal*
42. *3rd ventricle*
43. *Left lateral ventricle*
    a. posterior horn
    b. inferior horn
44. *Zygomatic arch*
45. *External acoustic meatus*
46. *Tympanic membrane*
47. *Mental foramen*
48. *Thyroid cartilage*
49. *Cricoid cartilage*
50. *Thyroid gland*
51. *Left lung*
52. *Trachea*
53. *2nd costal cartilage*
54. *Auricle of left atrium*
55. *Pulmonary valve*
56. *Aortic valve*
57. *Left border of heart*
58. *Left atrioventricular valve*
59. *Oesophagus*
60. *Stomach (empty)*
61. *Spleen*
62. *Pancreas*
63. *Duodenojejunal flexure*
64. *Left ureter*
65. *Descending colon*
66. *Aorta*
67. *Sigmoid colon*
68. *Umbilical cord*
69. *Median umbilical ligament*
70. *Umbilical artery*
71. *Common iliac artery*
72. *Urinary bladder*
73. *Ductus deferens at deep inguinal ring*
74. *Left seminal vesicle*
75. *Left half of prostate gland*
76. *Epididymis*
77. *Left testis*
78. *Scrotum*

4.5 Topographical representation of the anatomy of a full-term neonate (after Crelin, Functional Anatomy of the Newborn).

the diaphragm; it extends below the costal margin anteriorly, and in some cases to within 1 cm of the iliac crest posteriorly. The left lobe covers much of the anterior surface of the stomach and constitutes nearly one-third of the liver (**4.5, 6**). The liver is particularly large because of its precocious function as a site of haemopoiesis in the fetus; however, although its haemopoietic functions cease before birth its enzymatic and synthetic functions are not completely mature at birth.

Gallbladder. This has a smaller peritoneal surface than in the adult, and its fundus often does not extend to the liver margin. It is



4.6 Abdominal and thoracic viscera in situ in a full-term neonate. The anterior thoracic and abdominal wall has been removed. The lower abdominal wall has been deflected downwards.

generally embedded in the liver and in some cases may be covered by bands of liver. After the second year the gallbladder is of the relative size it is in the adult.

Pancreas (4.5). In the neonate this has all of the normal subdivisions of the adult. The head is proportionately larger in the newborn and there is a smooth continuation between the body and the tail. The inferior border of the head of the pancreas is found at the second lumbar vertebra; the body and tail pass cranially and to the left, and the tail is in contact with the spleen.

Peritoneal cavity (4.6). This is ovoid in shape in the neonate. It is fairly shallow from anterior to posterior as the bilateral posterior extensions each side of the vertebral column, which are prominent in the adult, are not present. Two factors lead to the protuberance of the anterior abdominal wall in the neonate and infant. Firstly, the diaphragm is flatter in the newborn, leading to a caudal displacement of the viscera compared to the adult. Secondly, the pelvic cavity is very small in the neonate and the organs which are normally pelvic in the adult, i.e. urinary bladder, ovaries and uterus, all extend superiorly into the abdomen (4.4). The pelvic cavity is joined to the abdominal cavity at less of an acute angle in the neonate as there is no lumbar vertebral curve and only a slight sacral curve.

Peritoneal attachments. These are similar to the adult; however, the greater omentum is relatively small; its constituent layers of peritoneum may not be completely fused and it does not extend much below the level of the umbilicus (4.4). Generally the length of the mesentery of the small intestine and of the transverse and sigmoid mesocolons are longer than in the adult, whereas the area of attachment of the ascending and descending colons is relatively smaller. The peritoneal mesenteries and omenta contain little fat.

RESPIRATORY SYSTEM

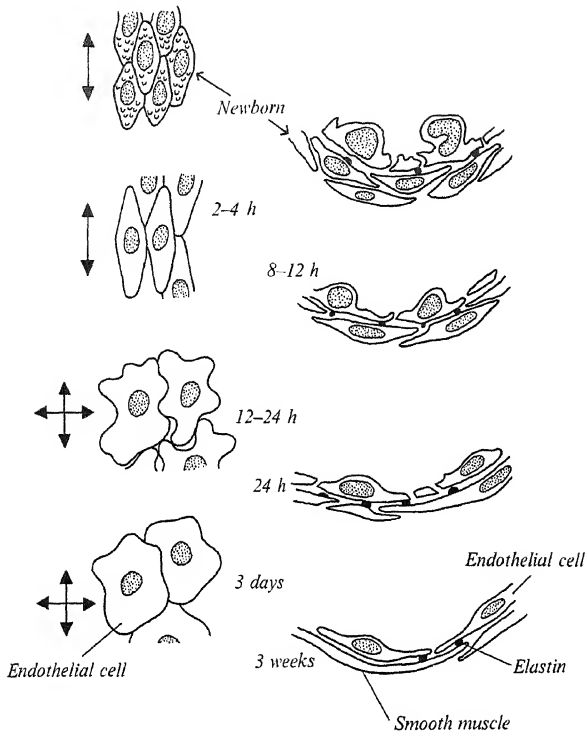
Trachea. This is relatively small in relation to the larynx in the neonate (4.5). The walls of the trachea are relatively thick and the tracheal cartilages are relatively closer together than in the adult. The ability of the trachea to resist external compression is about one-third that of a one-year-old infant, a fourth that of a five-year-old child, and a sixth that of an adult (Crelin 1973). The trachea commences at the upper border of C6; a relationship conserved with growth, it bifurcates at the level of the third or fourth thoracic vertebra.

Lungs. In the neonate these are relatively shorter and broader than those in the adult (4.5, 6). The respiratory rate in a full-term infant is 40–44 breaths/minute (normal resting rate in an adult male is 12/min). At birth the lungs are still in the alveolar stage of development (see p. 178); this continues through the neonatal period and into childhood perhaps up to 8 years of age although the time at which this stage is complete has not yet been established.

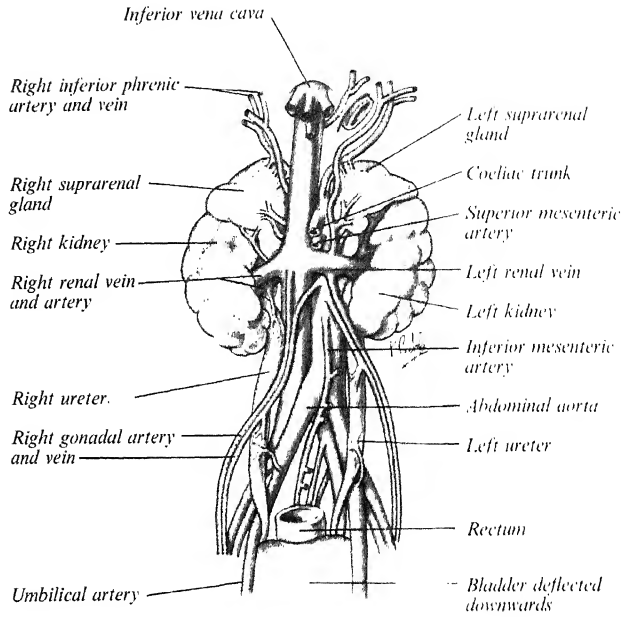
Normal postnatal pulmonary arterial development. Immediately after birth dramatic remodelling of the pulmonary vasculature occurs to effect an abrupt reduction of pulmonary vascular resistance. This process continues at a rapid rate throughout the first 1–2 months, while the lungs adapt to extrauterine life, and then more slowly throughout childhood. Failure to remodel in the presence of an anatomically normal heart leads to persistent pulmonary hypertension (Haworth 1992).

Normal postnatal pulmonary arterial development in the full-term neonate can be divided into three stages (taken from Haworth 1992):

Stage one. Lasting from birth to about 4 postnatal days, this stage concerns the immediate adaptation to extrauterine life. At birth the endothelial cells of the precapillary arteries are squat and have narrow bases on the subendothelium, a low surface:volume ratio, and many surface projections. Five minutes after birth the endothelial cells are thinner and gradually show less cell overlap; the surface:volume ratio increases, and few cell projections are seen. The vessel wall becomes thinner and the lumen diameter increases (4.7).



4.7 En face views (left) and transverse sections (right) showing the changes in the endothelial and smooth muscle cells of small muscular pulmonary arteries accompanying terminal bronchi from the neonatal period to three weeks after birth (from Haworth 1992).



4.8 Posterior abdominal wall of a full-term neonate. Note the lobulated kidneys and relatively wide calibre of the ureters (after Crelin, Anatomy of the Newborn: An Atlas).

The smooth muscle cells show a significant reduction in diameter during this time.

Stage two. From birth, particularly from day 4 to 3–4 weeks, the cells deposit matrix around themselves to fix their new positions. At birth the internal elastic lamina of the small muscular arteries consists only of amorphous elastin in a basal lamina-like matrix. By 3 weeks of age a definitive elastic lamina is evident; however, it is heavily fenestrated, permitting contact between the endothelial cells and the smooth muscle cells.

Stage three. This continues into adulthood. The intrapulmonary arteries increase in size and their walls increase in thickness. However, from birth all the pulmonary vascular smooth muscle cells from the hilum to the precapillary bed are immature; maturation is not advanced until 2 years.

As the distal airspaces expand there is a process of fusion of the capillary nets from one alveolus to another, forming, for a period, an extensive double capillary net. Fusion of these layers can be seen from 28 postnatal days and it becomes more extensive by 1.5 years; it is thought to be complete by 5 years.

The amount and type of connective tissue in the lung changes after birth. The neonatal lung has abundant type III and type IV collagen but little type I collagen, as seen in mature lungs. The former collagen types are not so strong, suggesting that the neonatal lung is more plastic; this would facilitate the changes in cell shape and orientation that characterize adaptation to extrauterine life. The rapid deposition of type I collagen postnatally gives structural stiffness to the blood vessel walls.

Thorax. Because it is relatively soft and flexible in the neonate, it makes the chest wall subject to collapse during negative pressure generation. The neonatal thorax has a round circumference rather than the dorsoventrally flattened profile of the adult.

At all ages during rapid eye movement (REM) sleep, there is a reduction if not a loss of tonic intercostal muscle activity. The mechanism is thought to be related to a descending spinal inhibition of the muscle spindle system. Further, there is often a destabilization of the chest wall which results in the rib cage and abdominal respiratory movements being out of phase. The neonate is at particular risk in this respect, firstly because the chest wall is flexible, and secondly, because much of the infant sleep activity is of the REM type (Woodrum 1992).

Diaphragm. To date this has not been well studied in the neonate. It is relatively flat at birth, gaining the dome shape with growth of the thorax and abdominal viscera. There is an exaggerated asymmetric movement of the neonatal diaphragm with the posterior portion showing a considerably greater excursion than the anterior portion. Thus the diaphragm after birth is potentially less effective in compressing the abdominal contents and expanding the lower thorax, having a flatter configuration and narrower zone of apposition, where the diaphragmatic fibres are parallel to the body axis and in direct contact with the lower rib cage (Woodrum 1992).

URINARY SYSTEM

Kidneys. At birth the two kidneys weigh about 23 g. They function early in development producing the amniotic fluid which surrounds the fetus. Fetal kidneys have a lobulated appearance which is still present at birth (4.5, 8). Addition of new cortical nephrons continues in the first few months of postnatal life after which the general growth of the glomeruli and tubules results in the disappearance of the lobulation.

The kidneys respond to the work load they are required to do; thus if one kidney is abnormal or removed, the remaining kidney becomes larger than the two kidneys combined would have done. The renal blood flow is lower in the neonate, the glomerular filtration rate at birth being approximately 30% that of the adult value; adult values for glomerular filtration are attained by 3–5 months of age and for renal blood flow by the end of the first year.

Urinary bladder. In the neonate this is egg-shaped with the larger end directed downwards and backwards (4.4, 5, 6, 9, 10). From the bladder neck the bladder extends anteriorly and slightly upwards in close contact with the pubis until it reaches the anterior abdominal wall. The apex of the contracted bladder is at a point midway between the pubis and the umbilicus; when the bladder is filled with urine the apex may extend up to the level of the umbilicus. There is no true fundus in the bladder as in the adult. The anterior surface is not covered with peritoneum; however, posteriorly peritoneum extends as low as the level of the urethral orifice. Although the neonatal bladder is described as abdominally placed, Symington (1887) noted that if a line is drawn from the promontory of the

sacrum to the upper edge of the pubic symphysis, nearly one half of the bladder is found below that line, i.e. within the cavity of the true pelvis. However, pressure on the lower abdominal wall will express urine from an infant bladder and the bladder does not gain its adult, pelvic, position until about the sixth year. The bladder remains connected to the umbilicus by the obliterated remains of the urachus; stimulation of the umbilicus can initiate micturition in babies. Because of the elongated shape of the bladder in neonates the ureters are correspondingly reduced in length and have no pelvic portion compared to adults. In the neonate a distinct interureteric fold is present in the contracted bladder.

REPRODUCTIVE SYSTEM

Reproductive organs in the female

Ovaries. The combined weight of the ovaries at birth is about 0.3 g; they double in weight during the first 6 postnatal weeks. The ovaries are relatively large at birth and much larger than the testes (4.5, 9). They have surface furrows which disappear during the second and third postnatal months. In the neonate the ovaries are found in the lower part of the iliac fossae; they complete their descent into the ovarian fossae in early childhood. The long axis of the ovary is almost vertical in the neonate, becoming temporarily horizontal during descent and vertical once more in the ovarian fossa. All of the primary oöcytes for the reproductive life of the female neonate are present in the ovaries by the end of the first trimester of pregnancy. Of the 7 000 000 primary oöcytes estimated at the fifth month of gestation 1 000 000 remain at birth; this is reduced to 40 000 by puberty and only 400 are ovulated during reproductive life.

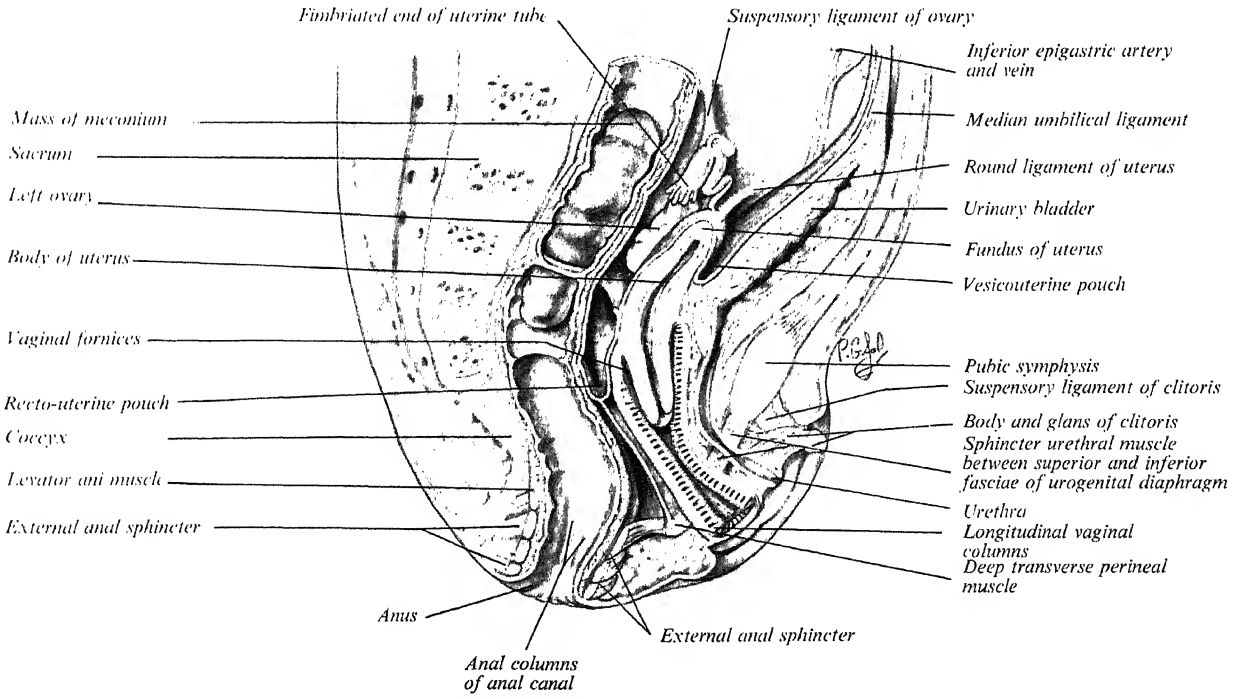
Uterus. At birth this is 2.5–5 cm long (average 3.5 cm), 2 cm wide between the uterine tubes, and about 1.3 cm thick (4.4, 5, 9). The body of the uterus is smaller than the uterine cervix which forms two-thirds or more of the length. The isthmus between the body and the cervix is absent. Generally the fetal female reproductive tract is affected by maternal hormones and undergoes some enlargement in the fetus. The endocervical glands are active before birth and usually the cervical canal is filled with mucus. After birth the uterus involutes, decreasing by about one-third in length and more than a half in weight. The neonatal size and weight of the uterus is not regained until puberty. The uterine tubes are relatively short and wide. The position of the uterus in the pelvic cavity depends to a great extent on the state of the bladder anteriorly and the rectum posteriorly. If the bladder contains only a small amount of urine the uterus may be anteverted but often it is in a direct line with the vagina.

Vagina. In the neonate this is about 2.5–3.5 cm long and 1.5 cm wide at the fornices. The uterine cervix extends into the vagina about 1 cm. The posterior vaginal wall is longer than the anterior giving the vagina a distinct curve (4.4, 9). The cavity is filled with longitudinal columns covered with a thick layer of cornified, stratified squamous epithelium. These cells slough off after birth when the effect of the maternal hormones is removed. The orifice of the vagina is surrounded by a thick elliptical ring of connective tissue, the hymen (4.9). During childhood the hymen becomes a membranous fold along the posterior margin of the vaginal lumen; should the fold form a complete diaphragm across the vaginal lumen it is termed an imperforate hymenal membrane.

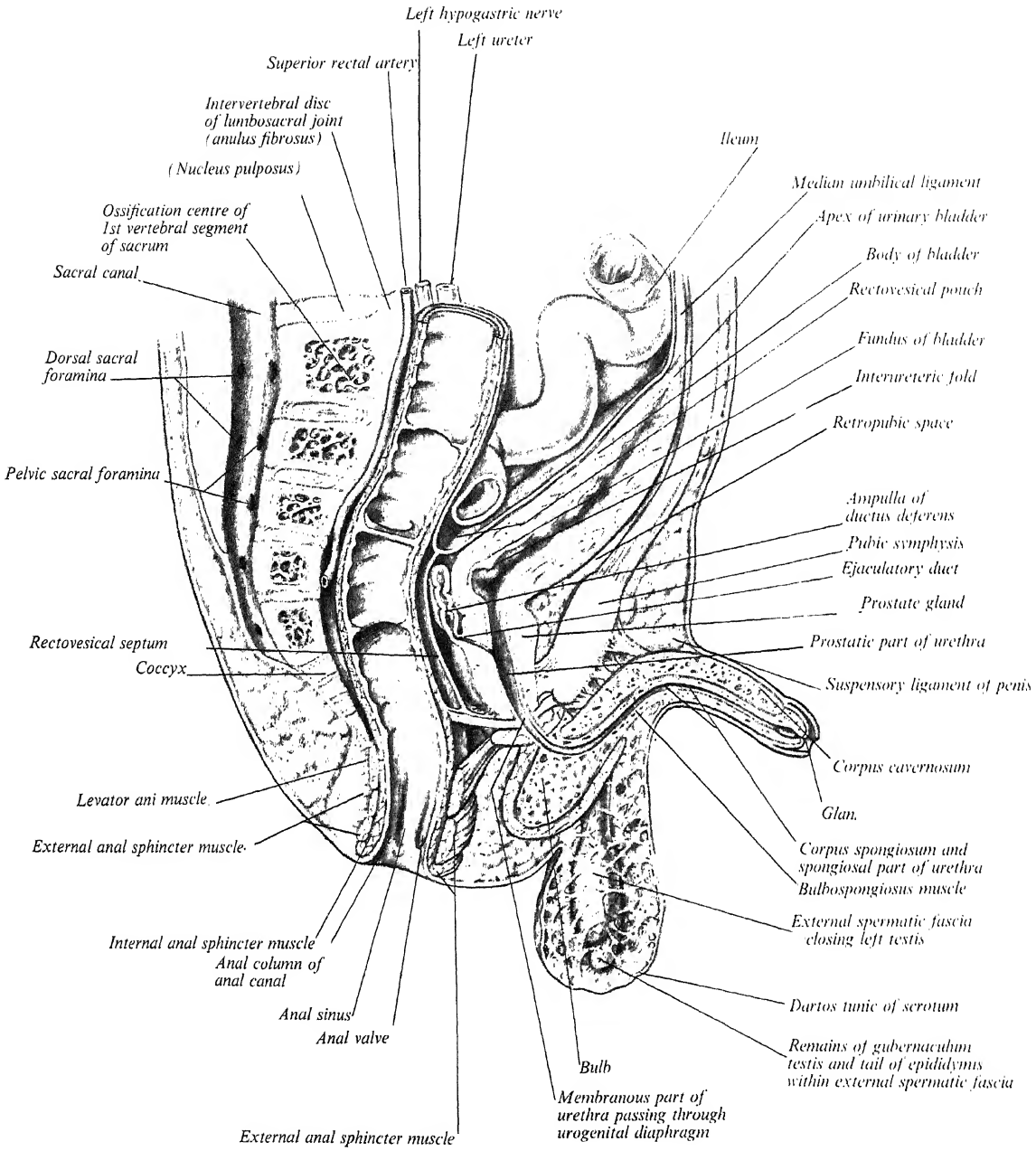
External genitalia. At birth these include relatively enlarged labia minora, clitoris and labia majora. The labia majora are united by a posterior labial commissure. They each contain the distal end of the round ligament of the uterus (the gubernaculum, see p. 213).

Reproductive organs in the male

Testes. These are relatively the same weight as in the adult. The long axis of the testis is almost vertical (4.5, 10). The testes are situated at the future deep inguinal rings by the sixth to seventh month of gestation. They descend into the scrotum before birth (see p. 212), the left testis usually migrating ahead of the right. In full-term male neonates 90% have descended testes; however, in premature babies descent may not be complete. The testes, unlike the ovaries, contain primordial germ cells which are surrounded by Sertoli cells preventing their further proliferation and meiosis until puberty. The processus vaginalis which precedes the testis in its descent into the scrotum is collapsed at birth but not necessarily obliterated. In 66% of male infants it remains patent for up to 2



4.9 Midsagittal section through the pelvis of a full-term female neonate. Note the abdominal position of the urinary bladder and uterus (after Crelin, Anatomy of the Newborn: An Atlas).



4.10 Midsagittal section through the pelvis of a full-term male neonate. Note the abdominal position of the urinary bladder (after Crelin, Anatomy of the Newborn: An Atlas) (see also **8.183**).

weeks. By between 10 and 20 days after birth the processus is partially (or completely) obliterated in 80% of male infants, the left side before the right. The *spermatic cord* is relatively large in the neonate as are the seminal vesicles and adjacent ampullae of the ductus deferens. The *prostate gland* (**4.10**) is similar to the uterine cervix of the female in shape, size and its position; it is the only major organ in the male neonatal pelvic cavity apart from the rectum.

Penis and scrotum. In the neonate these are relatively large. Although the prepuce and glans begin to separate from the fifth month in utero they may still be joined at birth. Despite containing less smooth muscle and elastic tissue than the adult, the neonatal penis is capable of erection. The scrotum has a broad base which does not narrow until after the first year. Both the septum and the walls of the scrotum are relatively thicker than in adults.

NERVOUS SYSTEM

Brain

The brain of the full-term neonate ranges from 300–400 g with an average of 350 g; the brains of neonatal males are slightly heavier than those of females. Because the head is large at birth, measuring one quarter the total body length, the brain is also proportionally larger, and constitutes 10% of the body weight (2% in the adult). The brain reaches 90% of its adult size by the fifth year, and 95% by 10 years. The sulci of the cerebral hemispheres appear from the fourth month of gestation (**3.122**) and at full term the general arrangement of sulci and gyri are present but the insula is not completely covered. The central sulcus is situated further rostrally and the lateral sulcus is more oblique than in the adult. Most of the

developmental stages of sulci and gyri have been identified in the brains of premature infants.

The pons is relatively smaller in the full-term neonate; the brainstem is more oblique and has a distinct bend as it passes through the foramen magnum to become the spinal cord. Of the cranial nerves, the olfactory and the optic at the chiasma are much larger than in the adult, whereas the roots of the other nerves are relatively smaller.

Spinal cord

The spinal cord in the neonate extends to L2 – L3; lumbar puncture investigations should thus never be attempted higher than the L3/L4 intervertebral space (see p. 22).

Myelination. This occurs over a protracted period beginning during the second trimester in the peripheral nervous system (PNS), with motor roots myelinating before sensory roots, and continuing in the central nervous system (CNS) where conversely the sensory nerves myelinate before the motor systems. The cranial nerves of the midbrain, pons and medulla oblongata begin myelination at about 6 months gestation. Myelination is not complete at birth; its most rapid phase occurs during the first 6 months of postnatal life, after which it continues at a slower rate up to puberty and beyond. The sequence of myelination of the motor pathways may explain, at least partially, the order of development of muscle tone and posture in the premature infant and neonate. Myelination of the various subcorticospinal pathways, i.e. vestibulospinal, reticulospinal, olivospinal and tectospinal (often grouped as bulbospinal tracts) occurs from 24–30 weeks gestation, for the medial groups, and extends to 28–34 weeks gestation for the lateral groups; lastly myelination of the corticospinal tracts occurs at term. Thus, in the preterm infant, axial extension precedes flexion, whereas finger flexion precedes extension. By term the neonate at rest has a strong flexor tone accompanied by adduction of all limbs. Neonates also display a distinct preference for a head position facing to the right, which appears to be independent of handling practices and may reflect the normal asymmetry of cerebral function at this age (Hill 1992).

The brain occupies 97.5% of the cranial cavity from birth to 6 years of age after which the space between the brain and skull increases until the adult brain occupies only 92.5% of the cranial cavity. Although the cerebral ventricles are larger in the neonate than in the adult, the newborn has a total of about 10–15 ml of cerebrospinal fluid when delivered vaginally and 30 ml when delivered by caesarian section.

Reflexes

A number of reflexes are present at birth and their demonstration is used to indicate normal development of the nervous system and responding muscles. Robinson (1966) noted that five tests of neurological development were most useful in determining gestational age. The pupillary reflex is consistently absent before 29 weeks gestation and present after 31 weeks; the glabellar tap, a blink in response to a tap on the glabella, is absent before 32 weeks and present after 34 weeks; the neck righting reflex appears between 34 and 37 weeks; the traction response, where flexion of the neck or arms occurs when the baby is pulled up by the wrists from the supine position appears after 33 weeks; head turning in response to light appears between 32 and 36 weeks. The spinal reflex arc is fully developed by the eighth week of gestation and muscle stretch reflexes at the knees and ankles may be elicited in premature infants of 19–23 weeks gestation. The Babinski response, which involves extension of the great toe with spreading of the remaining toes in response to stimulation of the lateral aspect of the sole of the foot, is elicited frequently in neonates; it reflects poor cortical control of motor function by the immature brain (Hill 1992).

The usual reflexes which can be noted in the neonate include Moro, asymmetric tonic neck response, rooting-sucking, grasp, placing (contacting the dorsum of the foot with the edge of a table produces a 'stepping over the edge' response), stepping, and trunk incurvation (elicited by stroking down the paravertebral area with the infant in the prone position). Examination of the motor system and evaluation of these reflexes allows assessment of the nervous system in relation to gestational age. The neonate also exhibits complex reflexes such as nasal reflexes and sucking and swallowing.

Nasal reflexes. These produce apnoea via the diving reflex, sneezing, sniffing, and both somatic and autonomic reflexes. Stimulation of the face or nasal cavity with water or local irritants produces apnoea in neonates. Breathing stops in expiration, with laryngeal closure, and infants exhibit bradycardia and a lowering of cardiac output. Blood flow to the skin, splanchnic areas, muscles and kidneys decreases, whereas flow to the heart and brain is protected. Different fluids produce different effects when introduced into the pharynx of preterm infants. A comparison of the effects of water and saline in the pharynx showed that apnoea, airway obstruction, and swallowing occur far more frequently with water than with saline, suggesting the presence of an upper airway chemoreflex (see Duara 1992). Reflex responses to the temperature of the face and nasopharynx are necessary for the commencement of pulmonary ventilation; local anaesthetic agents applied to the nasopharynx will prevent the onset of ventilation in newborn lambs. Midwives have for many years blown on the faces of neonates to induce the first breath.

Sucking and swallowing. This is a particularly complex set of reflexes, partly conscious and partly unconscious. As a combined reflex it requires the co-ordination of most of the 12 cranial nerves. The neonate can, within the first couple of feeds, suck at the rate of once per second, swallow approximately after five or six sucks, and breathe during every second or third suck. Air moves in and out of the lungs via the nasopharynx, and milk crosses the pharynx en route to the oesophagus without apparent interruption of breathing and swallowing, or significant misdirection of air into the stomach or fluids in the trachea (Herbst 1989).

Sucking. Although this develops, generally, slightly later than swallowing, mouthing movements have been detected in premature babies as early as 18–24 weeks gestation, and infants delivered at 29–30 weeks gestation make sucking movements a few days after birth; however, co-ordinated activities are not noted before 33–34 weeks. The concept of non-nutritive and nutritive sucking has been introduced (Wolf 1972) to account for the different rates of sucking seen in the neonate. Non-nutritive sucking, when rhythmic negative intraoral pressures are initiated which do not result in the delivery of milk, can be spontaneous or stimulated by an object in the mouth. This type of sucking tends to be twice as fast as nutritive sucking, the sucking frequency for non-nutritive sucking being 1.7 sucks/second in 37–38 week premature babies, 2 sucks/second in term neonates, and 2.7 sucks/second at 7–9 months postnatally. Corresponding times for nutritive sucking are about 1 suck/second in term neonates, increasing to 1.5 sucks/second by 7 months postnatally.

The taste of the fluid as well as nutrient content affects the efficiency of nutritive sucking in the early neonatal period. There is more sucking with milk than with 5% dextrose; however, sucking activities increased with solutions determined sweet by adult appraisal. Odour can also have some effect on sucking. If the nipples of anaesthetized female rat are washed it will cause a decrease in the number of pups attaching to nipples and an increase in the time between finding the nipple and attachment (see Herbst 1989).

Swallowing movements. First noted at about 11 weeks gestation, in utero fetuses swallow about 450 ml of amniotic fluid per day. Sucking and swallowing in premature infants (1700 g) is not associated with primary peristaltic waves in the intestine; however, in older babies and full-term neonates, at least 90% of swallows will initiate primary peristaltic waves.

In full-term neonates, the placing of a spoon or food onto the anterior part of the tongue elicits an extrusion reflex: the lips are pursed and the tongue pushes vigorously against the object. By 4–6 months the reflex changes and food deposited on the anterior part of the tongue is moved to the back of the tongue, into the pharynx, and swallowed. Rhythmic biting movements occur by 7–9 months postnatally, even in the absence of teeth.

Difficulties in suck and swallow. In infancy this may be an early indication of disturbed nervous system function. An interesting correlation between feeding styles of neonates and later eating habits has shown that children who were obese at 1 and 2 years of age, as measured by triceps skin-fold thickness, had a feeding pattern in the first month of life characterized by sucking more rapidly, producing higher pressures during prolonged bursts of sucking, and having shorter periods between bursts of sucking. Fewer feeds and higher sucking pressure were also associated with greater adiposity (Agras et al 1987).

CHROMAFFIN ORGANS

Suprarenal glands

The suprarenal glands are relatively very large at birth (4.5, 8) forming 0.2% of the entire body weight, compared with 0.01% in the adult. The left gland is heavier and larger than the right, as in the adult. At term each gland weighs about 4 g; the average weight of the two glands is 9 g (average in the adult is 7–12 g). The glands involute rapidly in the neonatal period with each gland losing 25% of its mass; the average weight of both glands is 5 g by the end of the second week, and 4.36 g by 3 months. The birth weight is not regained until puberty. The cortex of the suprarenal gland is thicker than in the adult and the medulla of the gland is small. Early studies on fetal suprarenal glands described extensive degeneration and necrosis within the fetal zone; however, it is believed that these studies showed disease processes rather than the normal involution of the gland. Normal involution causes the fetal zone cells of the postnatal gland to become smaller and assume the appearance and organization typical of zona fasciculata. In studies on neonatal monkeys a centripetal wave of transformation of fetal zone cells to zona fasciculata was observed, with only rare mitotic figures and no evidence of necrosis or collapse (Winter 1992).

MUSCULOSKELETAL SYSTEM

Fetal movements. These have been detected by ultrasonography in the second month of gestation (Hill 1992). Simple movements of an extremity have been observed sporadically as early as the seventh week of development (week 9 of pregnancy); combined movements of limb, trunk and head begin between weeks 12–16 of development. Fetal movements related to trunk and lower limb movements can be perceived consistently by the mother from about 16 weeks gestation (quickening). Movements of the fetus are often slow, asymmetric twisting and stretching movements of the trunk and limbs, resembling athetoid movements. Also there may be rapid, repetitive wide-amplitude limb movements, similar to myoclonus. By 32 weeks gestation symmetric flexor movements are most frequent and by term the quality of the movements has generally matured to smooth alternating movement of the limbs with medium speed and intensity. The reduced effect of gravity in utero may cause certain fetal movements to appear, on ultrasonography, more fluent than the equivalent movements observed postnatally. The number of spontaneous movements decreases after the 35th week of gestation and there is from this time an increase in the duration of fixed postures (Hill 1992). This restriction of normal fetal movements in late gestation is due to the degree of compliance of the maternal uterus; there is a slowing of growth at this time (see p. 26).

Early embryonic and fetal movements are vital to align the trabeculae within the bones, the correct attachments of the tendons, and the appropriate coiling of the constituent collagen fibres of the tendons. Movements of the fetus also encourage skin growth and flexibility indirectly as it is noted that fetuses with in utero muscular dystrophies, or other conditions resulting in small or atrophied muscles, have webs of skin, *pterygia*, passing across the flexor aspect of the joints. The condition, multiple pterygium syndrome, is characterized by webbing across the neck, the axillae and antecubital fossae. Usually the legs are maintained straight and webbing is not seen at the hip and knee.

The workload undertaken by the musculoskeletal system before birth is relatively light as the fetus is under essentially weightless conditions supported by the amniotic fluid. Thus the load on the muscles and bones is generated by the fetus itself with little gravitational effect. The reduction of gravitational force caused by the supporting fluid means that all parts of the fetus are subject to relatively equal forces and that the position assumed by the fetus relative to gravity is of little consequence. This is important to ensure the normal modelling of fetal bones especially the skull. Skulls of premature babies may become distorted due to the weight of the head on the mattress, despite regular changes in position; the application of oxygen therapy via a mask attached by a band around the head can cause dystososis of the occipital bone.

Neonatal skeleton

Generally the bones of the neonate are more spongy than the adult's because of the reduced work load undertaken by the fetus. Neonatal bones have more haemopoietic foci than adults': haemopoiesis occurs in the red marrow of all the bones of the skeleton but later becomes limited to the red marrow of the vertebral bodies, the ribs, sternum, diploë of the skull and proximal ends of the humerus and femur (see p. 1409).

Because the adult skeleton is composed of a number of bones which fuse after birth, the neonate technically has more bones (270) than the adult (206; 4.11).

Skull. The neurocranium is much larger than the viscerocranium in the neonate (4.12, 15, 28), the latter forming less than half of the length of the head, i.e. the distance from the top of the skull to the upper margin of the orbit is about 5 cm, whereas the distance from the upper margin of the orbit to the mandible is 4 cm. The ratio between the calvarial and facial portions is 8:1 at birth, changing to 2.5:1 in the adult female and 2:1 in the adult male. At birth the face is proportionally much wider than in the adult being twice as broad as its height.

Generally in the neonatal skull, the occipital condyles are elongate and flat instead of curved as in the adult. The tympanic rings are prominent features of the base of the skull; they provide attachment for the tympanic membranes (4.14, 15). The calvaria extends beyond the base of the skull both laterally and posteriorly. The hard palate is short (2.3 cm) and broad (2.2 cm) and the choanae are almost circular. The posterior border of the vomer at the choanae is relatively lower and more slanted than in the adult.

Fontanelles. The calvarial bones are thin at birth and ossification does not extend to the suture lines of the skull. The junctions between the calvarial bones are the sites of the fontanelles (4.13). Six fontanelles are present at birth; *anterior* and *posterior* fontanelles are median, paired *sphenoid* and *mastoid* are lateral, and other smaller accessory fontanelles may be present. An additional fontanelle located between the anterior and posterior fontanelles along the sagittal suture is found in some normal neonates but also in some infants with trisomy 21. The largest fontanelle is the anterior: it has an average diameter of 25 mm at birth. It overlies the superior sagittal dural venous sinus which transmits its pulsations to the overlying skin. Obliteration of the fontanelles occurs with progressive ingrowth of the edges of the bones that form their borders. The sphenoid is obliterated by 6 months as is the posterior; the anterior and mastoid are obliterated by the second year.

During parturition the calvarial bones can be displaced to the extent that they overlap each other at the sutures. Such skull 'moulding', occurring during delivery of the head, may exert tension on the great cerebral vein and be severe enough to rupture it.

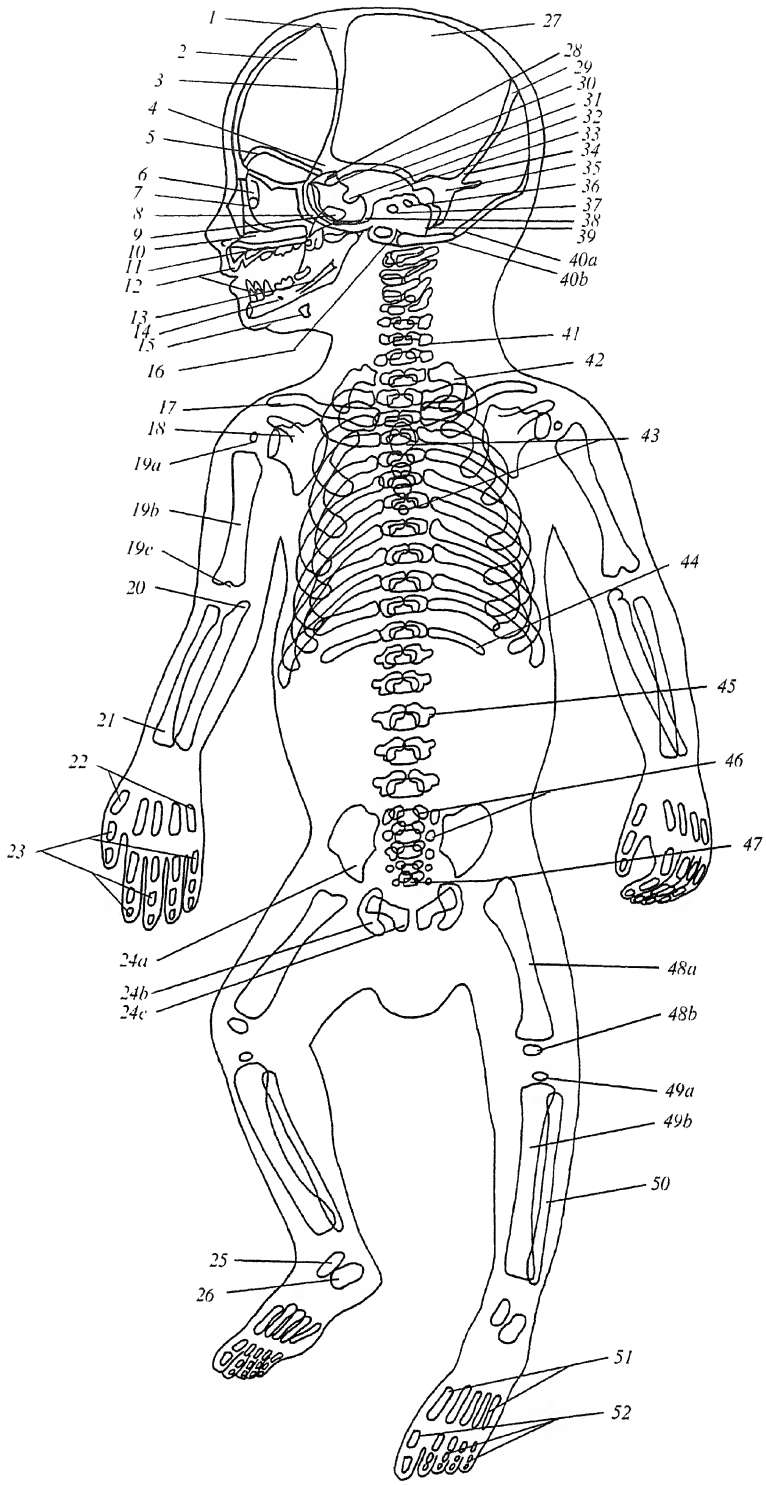
Frontal bones (4.12). These are separated by the metopic suture at birth; this is obliterated by 6–8 years. Frontal sinuses do not develop until the second postnatal year.

Ethmoid bone (4.16). This has only the lateral masses containing the ethmoid air cells ossified at birth; the remainder is cartilage. The part forming the upper portion of the nasal septum ossifies during the first year, the two cribriform laminae ossify in the second year and the crista galli between the second and fourth years. These cartilaginous portions of the ethmoid fuse as they ossify, joining with the lateral masses in the sixth year.

Sphenoid bone (4.16). Made up of three parts, body, lesser wings, and greater wings with the pterygoid processes, these composite parts fuse during the first year. A relatively large mass of cartilage separates the body of the sphenoid from the basilar part of the occipital bone at the spheno-occipital synchondrosis; union of these bones does not begin until shortly after puberty. The optic canal in the neonate is relatively large and has a keyhole or figure of 8 shape rather than the circular profile of the adult. Sinuses do not develop in the sphenoid until the fifth year.

Temporal bones (4.14, 15, 16). Each consists of four parts, squamous, petrous and tympanic separated by sutures and the styloid process. The squamous part has a shallow mandibular fossa and the articular tubercle is absent. The petrous part is relatively large. The tympanic ring is thin and incomplete, with ends fused with the squamous part. The styloid process is cartilaginous except for a small ossified portion near the proximal end. The mastoid process is

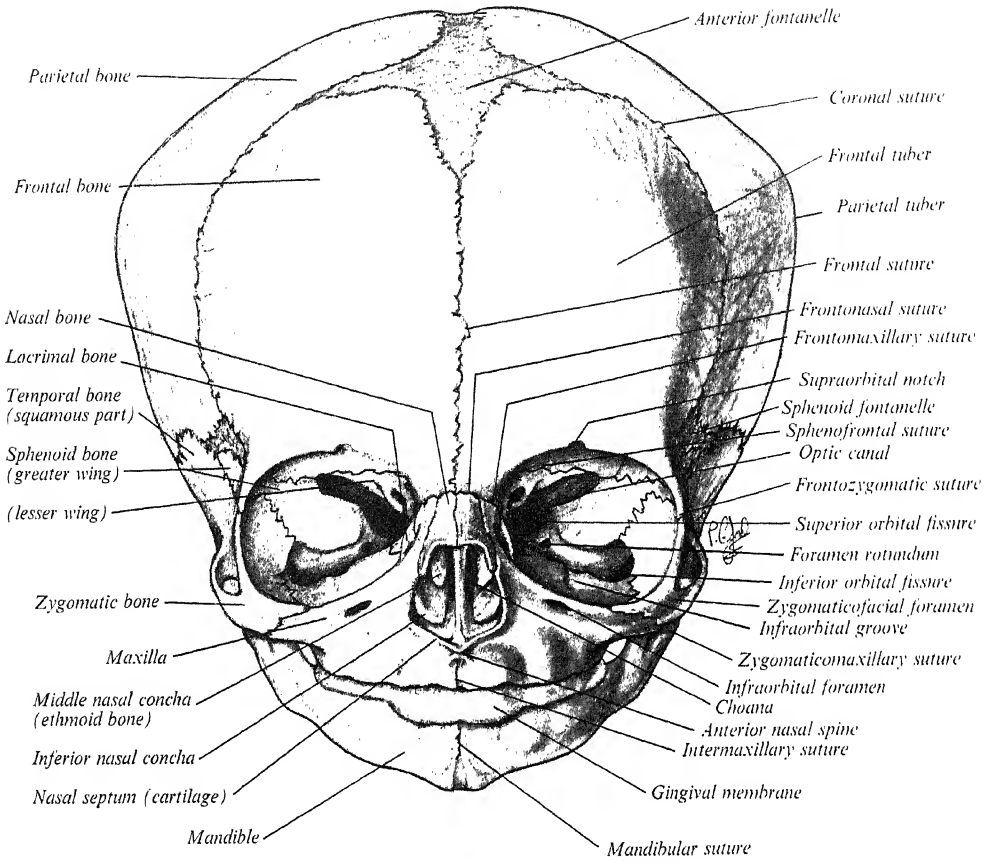
1. *Anterior fontanelle*
2. *Frontal bone*
3. *Coronal suture*
4. *Sphenoid fontanelle*
5. *Roof of orbit*
6. *Fossa for lacrimal sac*
7. *Nasolacrimal canal*
8. *Floor of middle cranial fossa*
9. *Pterygoid process*
10. *Infraorbital foramen*
11. *Hard palate*
12. *Enamel of deciduous teeth*
13. *Mandibular canal*
14. *Mental foramen*
15. *Body of hyoid bone*
16. *Tympanic part of temporal bone*
17. *Clavicle*
18. *Scapula*
19. *Humerus*
    a. *head*
    b. *body*
    c. *olecranon fossa*
20. *Ulna*
21. *Radius*
22. *Bodies of metacarpal bones*
23. *Bodies of phalanges*
24. *Coxal bone*
    a. *ilium*
    b. *ischium*
    c. *pubis*
25. *Centre in talus*
26. *Centre in calcaneus*
27. *Parietal bone*
28. *Lesser wing of sphenoid bone*
29. *Posterior fontanelle*
30. *Optic canal*
31. *Squamosal suture*
32. *Hypophyseal fossa of sphenoid bone*
33. *Squamous part of temporal bone*
34. *Lambdoidal suture*
35. *Mastoid fonticulus*
36. *Subarcuate fossa*
37. *Internal acoustic meatus*
38. *Spheno-occipital synchondrosis*
39. *Petrous part of temporal bone*
40. *Occipital bone*
    a. *squamous part*
    b. *lateral part*
41. *6th cervical vertebra (3 centres)*
42. *1st rib*
43. *Centres of sternum (superimposed upon thoracic vertebrae)*
44. *12th rib*
45. *3rd lumbar vertebra (3 centres)*
46. *Centres in sacrum*
47. *Centre in coccyx*
48. *Femur*
    a. *body*
    b. *condylar centre*
49. *Tibia*
    a. *condylar centre*
    b. *body*
50. *Fibula*
51. *Bodies of metatarsal bones*
52. *Bodies of phalanges*



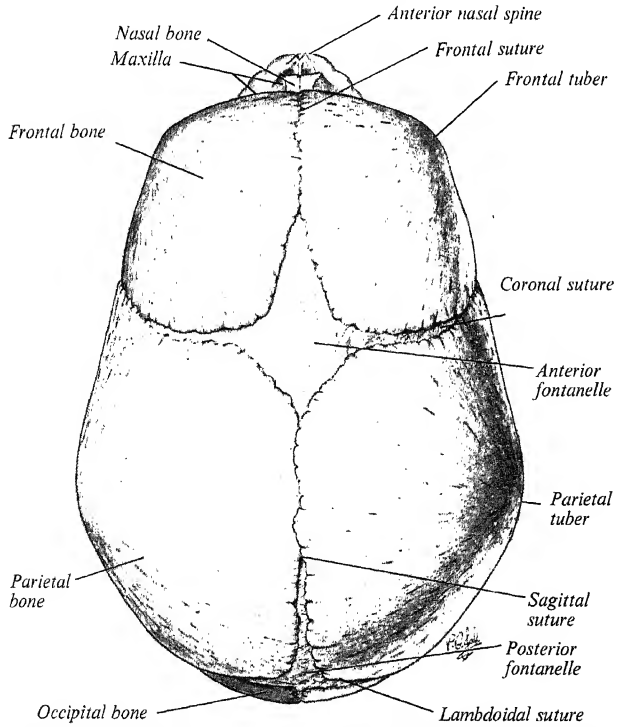
4.11 Ossified portions of the full-term neonate skeleton (after Crelin, Anatomy of the Newborn: An Atlas).

absent at birth; it develops as a small projection at the end of the first year; mastoid air cells invade it at puberty. In the neonate the petrous and squamous parts of the temporal bone are usually partially separated by the petrosquamous fissure which opens directly into the mastoid antrum of the middle ear. The fissure closes in 4% of infants during the first year but remains unclosed in 20 to 40% up to 19 years. It is a route for the spread of infection from the middle ear to the meninges.

External acoustic meatus. This is relatively long in the neonate, about two-thirds the length in the adult. It is almost straight and courses inward, downward and slightly forward. The lumen of the middle part is very narrow. The middle ear cavity is about the same size as the adult's. The epitympanic recess and the mastoid antrum are well developed. The auditory ossicles reach their adult size in the fetus by 6 months. The bony and membranous labyrinths of the inner ear are almost equal to adult size in the neonate; thus the inner



4.12 Anterior aspect of the full-term neonatal skull (after Crelin, Anatomy of the Newborn: An Atlas). For a comparative view of an adult skull see 6.135A, B.



4.13 Superior aspect of the full-term neonatal skull (after Crelin, Anatomy of the Newborn: An Atlas). For a comparative view of an adult skull see 6.137.

ear occupies a relatively greater area of the petrous part of the temporal bone.

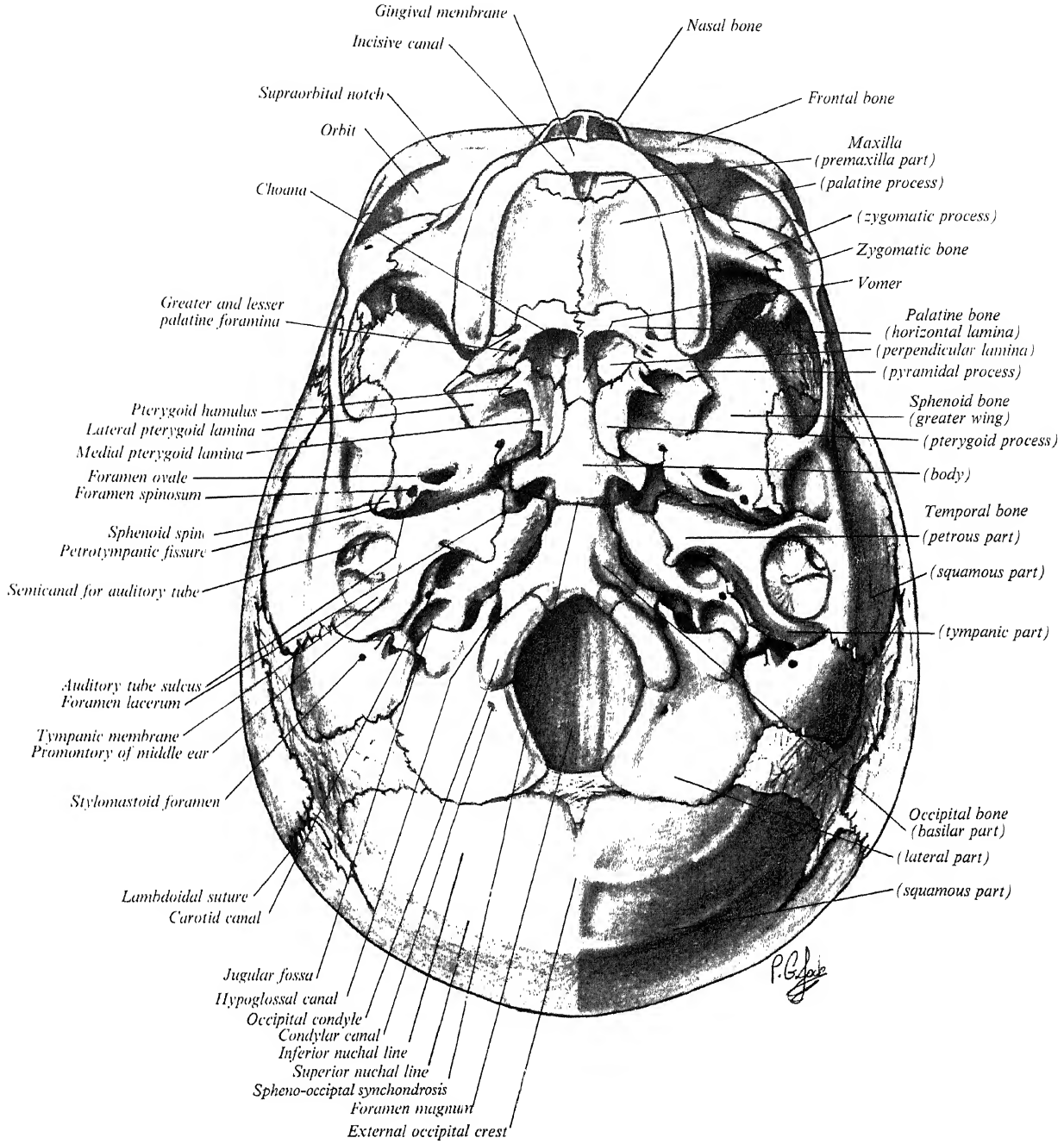
Internal acoustic meatus. The diameter of this in the neonate is almost as large as in the adult.

Auditory tube. In the neonate this is about half the length of the adult's; its opening from the middle ear cavity is as large as in the adult, but the pharyngeal opening in the nasal part of the pharynx is relatively smaller. The course of the auditory tube is horizontal in the newborn whereas in the adult it passes from the middle ear downward, forward and medially.

Occipital bone (4.11, 14, 15, 16). At birth this consists of four separate parts, a basilar part, two lateral parts and a squamous part; they are joined by cartilage and form a ring around the foramen magnum. The squamous and lateral parts fuse together from the second year; the cartilage between them is flexible at birth. The lateral parts fuse with the basilar part during years 3 and 4, but fusion may be delayed until the 7th year.

Maxillae (4.11, 12, 15, 16). These are low and broad with 10 large alveoli containing deciduous teeth. The bony palate is shallow at birth. Postnatal growth occurs mainly vertically. The maxillary sinus is an elongated sac in the neonate, but with eruption of the deciduous teeth it enlarges to become three times longer anteroposteriorly and five times greater in height and width. At birth the floor of the sinus is above that of the nasal cavity; in the adult it is below it.

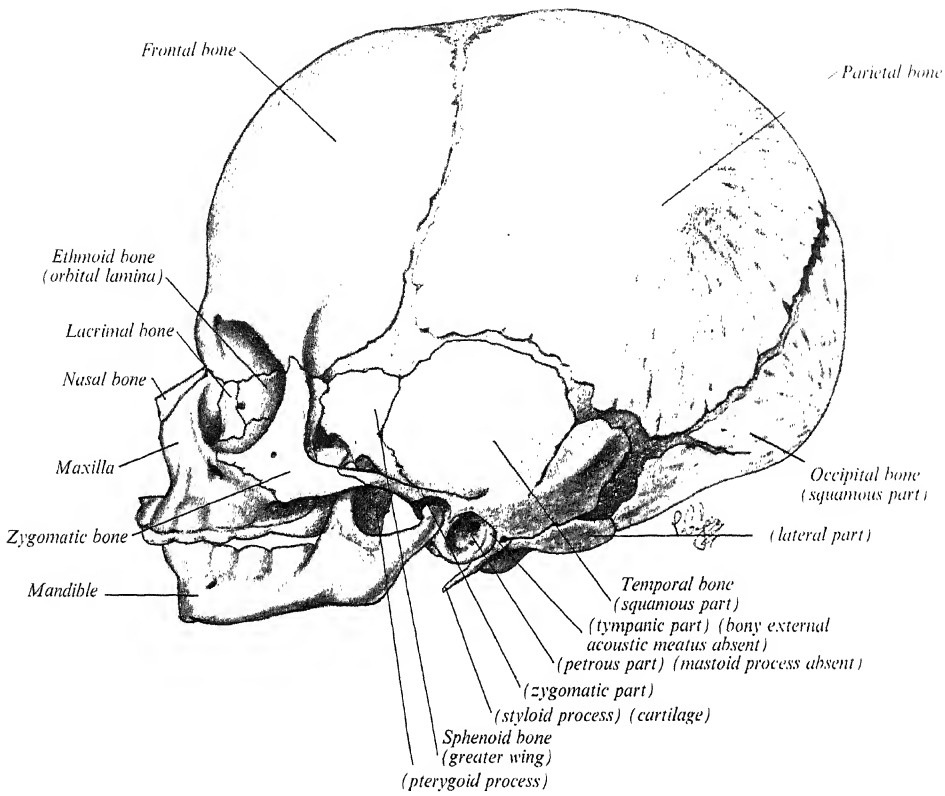
Mandible (4.11, 12, 15, 16). This is formed by two halves joined by fibrous tissue at the mandibular suture which fuse after the first year. The body of the mandible is relatively large; its upper two-thirds are filled with alveoli containing the deciduous and some permanent teeth. The rami are short and broad, at an angle of 140° to the body (120° in the adult); the rami are shorter than the body (same length in the adult).



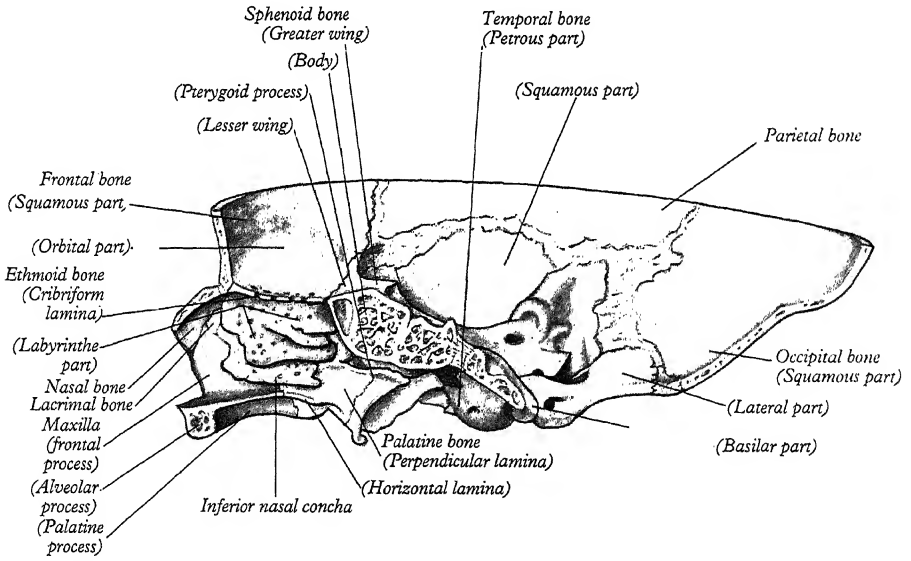
4.14 Inferior surface of the base of the full-term neonatal skull with the mandible removed (after Crelin, Anatomy of the Newborn: An Atlas). For comparative view of an adult skull see 6.141A, 144A.

Vertebral column. This has no fixed curvatures in the neonate (4.4, 11). Crelin (1973) notes that the vertebral column of the newborn is so flexible that when dissected free from the body it can easily be bent (flexed or extended) into a perfect half circle. A slight sacral curvature can be seen in the neonate; this develops as the sacral vertebrae ossify and fuse. The thoracic part of the column is the first to develop a relatively fixed curvature, concave anteriorly. The other curvatures develop later, the cervical curvature when the head can be held erect (from 3 months) and the lumbar curvature when walking starts (from 1 year). Each vertebra (excluding C1 and C2) consists of hyaline cartilage with three separate ossification centres. The atlas has only two ossification centres; it becomes a bony ring between the fifth and ninth years. The axis has four ossification centres, one for the body, two for the neural arches and one for the dens; the latter fuse between the third and sixth years. In the neonate the intervertebral discs are composed mainly of the nucleus pulposus which becomes much reduced in the adult as the annulus fibrosus develops.

Upper limbs. Generally the upper limbs are proportionately shorter than in the adult. They are long compared to the neonatal trunk and lower limbs, extending to the upper thigh as in the adult; but the trunk is much shorter in the neonate (4.11). At birth the upper limbs are about the same length as the lower limbs but much more developed. When examining the proportions of parts of the upper limb, the forearm is longer than the arm in the newborn, more so in boys than girls (p. 29). Only primary centres of ossification are present in the upper limb, apart from a centre in the head of the humerus. The elbow of the newborn cannot achieve full extension, being some 10–15% short; it can flex to 145°. Crelin (1973) notes that



4.15 Lateral view of a full-term neonatal skull (after Crelin, Anatomy of the Newborn: An Atlas). See also **6**.197. For a comparative view of an adult skull see **6**.133A, B.



4.16 Midsagittal section through a full-term neonatal skull (after Crelin, Anatomy of the Newborn: An Atlas). A sagittal section of an adult skull is presented in **6**.158.

the neonatal hand clearly shows four distinct palmar interosseous muscles, the deep head of flexor pollicis brevis being the first palmar interosseous, with a different origin and innervation to the superficial head of flexor pollicis brevis. The neonate has a relatively strong grasp, which may allow it to be pulled off a mattress within the first few days. The fingernails of the upper limb usually extend to the finger tips or just beyond; they are soft at birth but soon dry to become quite firm and sharp.

Pelvis. In the newborn the pelvis is cone-shaped; the transverse diameter of the true pelvis is 2.2 cm, its anteroposterior diameter

2.8 cm and its length between the inlet and outlet is 2 cm. The sacrum is proportionately larger than in the adult and the sacral promontory is higher. When walking commences the sacrum descends between the ilia and the promontory develops. The bilateral ilia, ischia and pubic bones are variably ossified (see p. 669) at birth; they meet at the acetabulum which in the neonate is cartilaginous, relatively large and shallow.

Lower limbs. Compared to the upper limbs these are underdeveloped. They are retained in a flexed position. The leg is proportionately shorter than the thigh. In the neonate the legs appear to be bowed; however, the tibia and fibula are straight and the illusion of bow-legs is caused by the shape of the soft tissues and the slightly more advanced development of the lateral head of the gastrocnemius compared to its medial head. The femoral neck is much shorter and forms an acute angle with the shaft. The shaft of the femur is quite straight; the curvature seen in the adult is acquired with walking. The head of the femur is larger than the acetabular fossa with nearly one-third remaining external; the ligamentum teres is relatively very long. Dislocation of the hip joint is relatively easy and the femoral head can be removed from the acetabular fossa laterally, but not posteriorly; such dislocation occurs more frequently on the right side and in caucasian females. Two of the tarsal bones, the calcaneus and the talus, have an ossification centre at birth and in 50% of neonates a centre is present in the cuboid.

The muscles of the lower limb are much less developed than those in the upper limb. The fetal position, often assumed by postnatal babies, keeps the thighs in continuous abduction, stretching the adductors. The muscles which will later be used for walking are weak and the lack of gluteal development, particularly, gives the typically diminutive buttocks of the neonate.

Feet. In neonates these are usually inverted. They have a greater degree of dorsiflexion caused by the relatively greater area of the trochlea of the talus; plantar flexion on the other hand is limited, due to some extent to the shortness of the extensor muscles of the foot. At birth the footprint outlines the whole plantar surface due to deposition of subcutaneous fat beneath the longitudinal and transverse arches; thus most babies appear flat-footed.

SKIN

The surface area of the skin increases with growth. It has been estimated that the surface area of a premature neonate weighing 1505 g is about 1266 cm^2, whereas a neonate of 2980 g has a surface area of 2129 cm^2. The skin of the neonate is thinner than that of older infants and children. It cornifies over a period of 2–3 weeks providing protection; however, in the premature infant the thin epidermal layer allows absorption of a variety of substances, for example chlorhexidene and boric acid. At birth the skin is richly vascularized by a dense subepidermal plexus. The mature pattern of capillary loops and of the subpapillary venous plexus is not present at birth but develops as a result of capillary budding with migration of endothelia at some sites and the absorption of vessels from other sites (Ryan 1992). Perera et al (1970) studied the microvasculature of the skin for the first 3 months of postnatal life and noted how some regions mature faster than others. They noted, inter alia, that with the exceptions of the palms, soles and nail beds, the skin of the neonate has almost no papillary loops; the skin has a disordered capillary network which becomes more orderly from the second week when papillary loops appear; defined loops are not present until the fourth or fifth week, but all areas possess loops by 14–17 weeks postnatally.

Neonates exhibit a regional sequence of eccrine gland maturation, with the earliest sweating occurring on the forehead, followed by the chest, upper arm and, later, more caudal areas. Acceleration of maturation of the sweating response occurs in premature babies after delivery (Lane 1992).

CARDIOVASCULAR AND LYMPHATIC SYSTEMS

Heart

The heart is relatively large at birth (**4.6, 17**), and weighs about 20 g; the cardiac output is about 550 ml/minute, and the blood pressure 80/46. The fetal heart rate is approximately 150 beats a minute near term, at birth it is about 180/minute and it drops over the neonatal period to 170/minute after about 10 minutes, 120–140/minute from 15 minutes to 1 hour after birth. Obviously any signs of fetal distress will increase this general, basic level. The heart rate drops further with increasing age; thus it is normally between 113 and 127 beats/minute from 6 months to 1 year, settling to about 100/minute by the end of the first year.

At all ages the interventricular septum is considered part of the left ventricle, and the heart ratio is expressed as: weight of left ventricle and septum/weight of right ventricle. At birth the left ventricle weighs about 25% more than the right; however, the right ventricle has been working against the systemic pressure in the fetus (the pulmonary circulation being not yet active) and there is a right ventricular functional preponderance in the first 2 or 3 months after birth. With the establishment of the pulmonary circulation the work of the right side of the heart decreases; the left side of the heart, particularly the ventricle, grows rapidly to meet the demands of the active neonate and by the end of the second year it weighs twice as much as the right, a condition which continues to middle age.

Corresponding to the weight differential between the right and left ventricles, at birth the average thickness of the lateral walls of the ventricles is about equal (5 mm). By the end of the third month the left ventricle is thicker than the right, becoming twice as thick by the second year and three times as thick by puberty.

The heart is situated in the neonate midway between the crown of the head and the lower level of the buttocks (**4.5**). The anterior surface is formed mainly by the right atrium and right ventricle as in the adult; this surface is usually covered by the thymus which may extend over the base of the right ventricle.

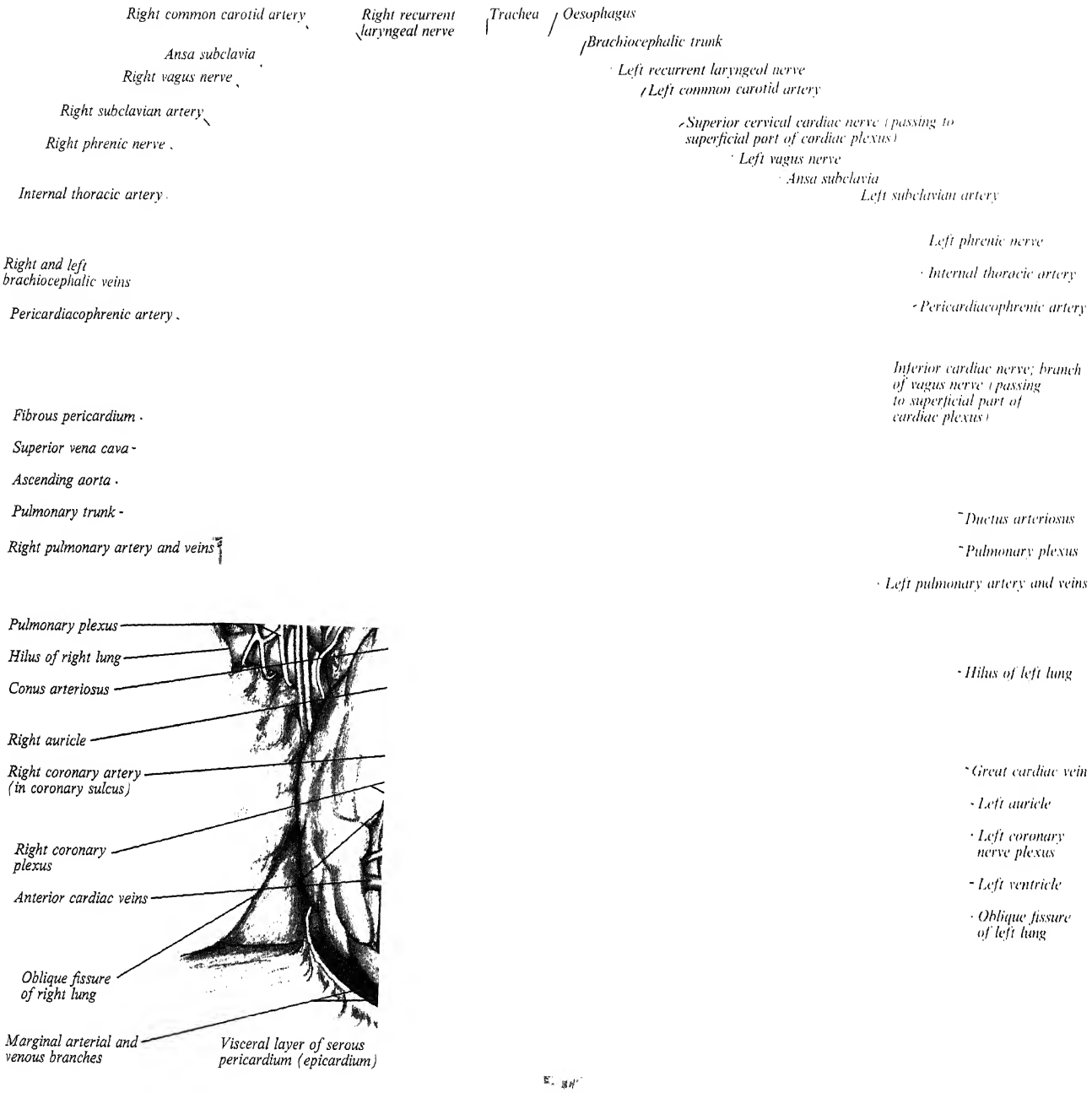
Foramen ovale. About 4–6 mm in vertical length and 3–4 mm wide, it lies at the level of the third intercostal space with its long axis in the median plane (**4.5**). It is almost exactly in the coronal plane of the body; thus blood passes from the anteriorly placed right atrium posteriorly and upwards to reach the upper, posterior part of the left atrium. Although the foramen ovale closes functionally after pulmonary respiration is established it does not become structurally closed until some time later. It is obliterated in less than 3% of infants 2 weeks after birth, but in 87% by 4 months after birth.

Occlusion of fetal vessels after birth

Soon after birth a number of fetal vessels occlude, but the majority of vessels do not, suggesting that the walls of a population of fetal vessels are different to the remaining vessels permitting their differential constriction. In many cases the tunica media contains populations of smooth muscle, elastic fibres and connective tissue which proliferate prior to birth. Bradykinin, one of the Kinins—polypeptide hormones that induce contraction or relaxation of smooth muscle—, forms in the blood of the umbilical cord when the temperature of the cord drops at or shortly after birth. It is also formed and released by granular leucocytes in the lungs of the neonate after exposure to adequate oxygen. Bradykinin is a potent constrictor of the umbilical arteries and veins and the ductus arteriosus, while being at the same time a potent inhibitor of contraction of the pulmonary vessels (Crelin 1973). It has long been realized that intact endothelium is required for the relaxation response to bradykinin.

Ductus arteriosus. The ductus arteriosus (**4.17, 18**) shunts blood from the pulmonary trunk in the fetus to the arch of the aorta, thus bypassing the lungs. It arises as a direct continuation of the pulmonary trunk where it divides into right and left pulmonary arteries; it is 8–12 mm long. It joins the aorta at an angle of 30–35° on the left side, anterolaterally, below the origin of the left subclavian artery. The opening of the ductus arteriosus into the aorta is greatly elongated. The diameter of the ductus at its origin from the pulmonary trunk, when distended with blood, is 4–5 mm; this is nearly equal to the diameter of the adjacent ascending aorta (5–6 mm). Both arteries taper to a smaller diameter as they pass inferiorly with the aorta remaining slightly larger (4 mm; **4.18**). In the neonate the ductus arteriosus is closely related to the left primary bronchus inferiorly and the thymus gland anteriorly.

The ductus arteriosus is very different from the other great vessels arising from the heart (see p. 314). All the other great vessels develop tunicae mediae which are elastic in nature whereas the ductus has a muscular morphology (de Ruiter et al 1990). It has been proposed



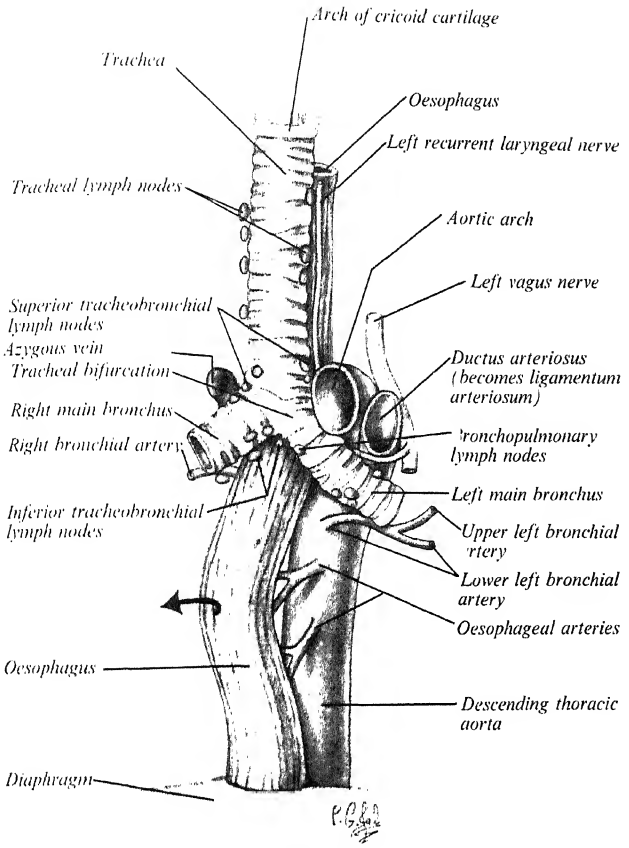
4.17 Anterior view of heart and great vessels in a full-term neonate. The lungs have been displaced to expose the heart and the epicardium dissected off the heart and roots of the great vessels (after Crelin, Anatomy of the Newborn: An Atlas).

that a relationship between the recurrent laryngeal branch of the vagus nerve and the developing ductus arteriosus could account for the histological difference in the ductus (Leonard et al 1983). The vagus nerve in the stage 16 embryo is very large in relation to the aortic arch system. The recurrent laryngeal nerve has a greater proportion of connective tissue than other nerves making it more resistant to stretch. Leonard et al (1983) suggest that tension applied by the left recurrent laryngeal nerve wrapping around the ductus arteriosus could provide a means of support which may permit the ductus to develop as a muscular artery rather than an elastic artery.

Patency of the ductus arteriosus. This is essential for fetal life. Prostaglandins appear to play a role in maintaining this patency. Fetal and neonatal ductal tissue can produce prostaglandin E_2 (PGE_2), prostaglandin I_2 (PGI_2), prostaglandin F_{2a} (PGF_{2a}). They inhibit the ability of the ductus to contract in response to oxygen.

Closure of the ductus arteriosus. Closure starts immediately after birth. The first stage is completed within 10–15 hours and the second stage takes 2–3 weeks. The first stage consists of contraction of the smooth muscle cells and development of subendothelial oedema; destruction of the endothelium and proliferation of the intima subsequently occurs, leading to permanent closure. Diverse factors have been identified which may promote ductal closure and include: increased oxygen tension; increase in the plasma catecholamine levels; suppression of PGI_2 production; switching off PGE receptors; a synergistic role of PGF_{2a} and oxygen levels; a fall in plasma adenosine level.

After birth these interrelated events together result in the closure of the ductus. It has been proposed that high oxygen tension initiates the synthesis of a hydroperoxy fatty acid which suppresses prostacyclin production, thus exposing the ductus to the contractile



4.18 Anterior view with the heart removed to show the relationship between the left primary bronchus, the aortic arch and the ductus arteriosus in a full-term fetus (after Crelin, Anatomy of the Newborn: An Atlas).

effects of prostaglandin endoperoxide. For a discussion of the factors associated with closure of the ductus see Mathew (1992).

Umbilical vessels

Umbilical arteries (4.5). These are in direct continuation with the internal iliac arteries. Their lumen is about 2–3 mm in diameter at their origin, when distended, narrowing as they approach the umbilicus with a reciprocal thickening of the tunica media due particularly to an increase in the number of longitudinal smooth muscle fibres and elastic fibres. Before birth there is a proliferation of connective tissue within the vessel wall. After the cord is severed the umbilical arteries contract preventing significant blood loss; thrombi often form in the distal ends of the arteries. The arteries obliterate from their distal ends until by the end of the second or third month involution has occurred at the level of the superior vesical arteries. The proximal parts of the obliterated vessels remain as the medial umbilical ligaments.

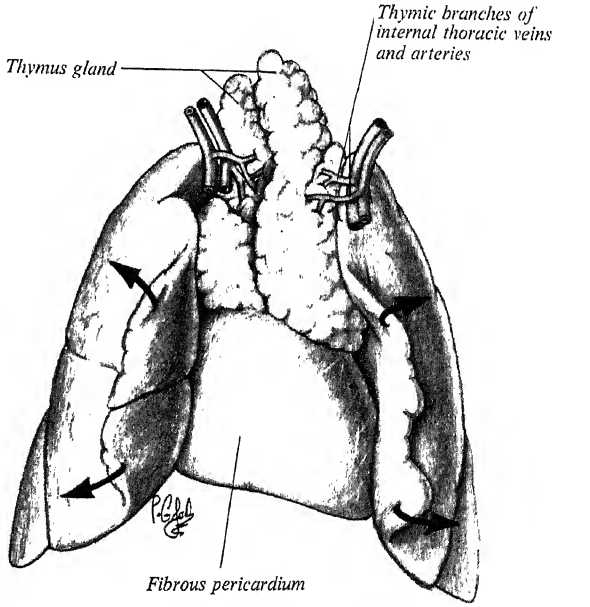
Umbilical vein (4.4, 5). In the neonate this is 2–3 cm long and 4–5 mm in diameter when distended. It passes from the umbilicus, within the layers of the falciform ligament, superiorly and to the right, to the porta hepatis. Here it gives off several large intrahepatic branches to the liver and then joins the left branch of the portal vein. The umbilical vein is thin walled; it possesses a definite internal lamina of elastic fibres at the umbilical ring, but not in its intra-abdominal course. The tunica media contains smooth muscle fibres, collagen and elastic fibres. When the cord is severed the umbilical vein contracts but not so vigorously as the arteries. The rapid decrease in pressure in the vein after the cord is clamped means that the elastic tissue at the umbilical ring is sufficient to arrest any retrograde flow along the vessel. Prior to birth there is a subintimal proliferation of connective tissue around the periphery of the lumen. After birth the contraction of the collagen fibres in the tunica media and the increased connective tissue constitute the ligamentum teres, obliteration of the vessel occurring from the umbilical ring towards the hepatic end; no thrombi are formed in the obliteration process. For up to 48 hours after birth the intra-abdominal portion of the umbilical vein can be easily dilated and in most adults the original lumen of the vein persists through the ligamentum teres and can be dilated to 5–6 mm in diameter.

Ductus venosus. This is a direct continuation of the umbilical vein arising from the left branch of the portal vein, directly opposite the termination of the umbilical vein. The ductus venosus passes for 2–3 cm within the layers of the lesser omentum, in a groove between the left lobe and caudate lobe of the liver, before terminating in the inferior vena cava, or in the left hepatic vein immediately before it joins the inferior vena cava. The tunica media of the ductus venosus contains circularly arranged smooth muscle fibres, an abundant amount of elastic fibres and some connective tissue. Obliteration of this vessel is initiated at the portal vein end and passes to the vena cava; it begins in the second postnatal week and the lumen is completely obliterated by the second or third month after birth.

Major arterial and venous vessels of the trunk. These, with their associated visceral branches, are relatively larger than those in the limbs, favouring central pooling of blood. Vessels in the periphery are nearly microscopic in the neonate and cannulation poses much more of a problem than in the adult. Large vessels are in the same relative positions as in the adult but may correspond to different vertebral levels. Thus although the bifurcation of the common carotid artery into the internal and external carotid arteries occurs at the level of the hyoid bone, as in the adult, the hyoid bone is relatively higher in the neonate neck than in the adult. The renal arteries similarly arise higher, often between T12 and L1 (in the adult upper border of L2). The abdominal aorta bifurcates into common iliac arteries at the upper border of L4 rather than at the lower border as in the adult.

Lymphoid and lymphatic tissues

Thymus (4.19). This accounts for 0.42% of the body weight at birth, compared to 0.03 to 0.05% in the adult. It weighs 10 g in the full-term neonate, increases in weight steadily until puberty, when it weighs about 30 g, and thereafter slowly decreases until old age when it may be 12.5 g. At birth the thymus is most often bilobar; it is 4–6 cm long, 2.5–5 cm wide and 1 cm thick. The gland has a cervical portion which may extend as high as the lower margin of the thyroid gland, inferiorly; the lower end of the right lobe is commonly between the right side of the ascending aorta and the right lung, anterior to the superior cava. Anterior to the gland in the neck are the sterno-hyoid and sternothyroid muscles and fascia; in the thorax the gland is covered by the manubrium, the internal thoracic vessels, the upper three costal cartilages, and laterally the pleura. Posteriorly the thymus



4.19 Anterior view of the thymus gland in the full-term neonate. The lungs have been displaced to show the extent of the gland (after Crelin, Anatomy of the Newborn: An Atlas).

is in contact with the vessels of the superior mediastinum, especially the left brachiocephalic vein which may be partly embedded in the gland, the upper part of the thoracic trachea, and the upper part of the anterior surface of the heart. The thickest part of the gland at birth is not at the superior thoracic aperture but lies immediately above the base of the heart. During childhood the thymus narrows and lengthens and the cervical portion becomes less noticeable. The thymus is necessary for the development of the white pulp of the spleen.

Spleen (4.5). At birth the spleen weighs, on average, 13 g. It doubles its weight in the first postnatal year and triples it by the end of the third year. Accessory spleens are very common in neonates, located in the greater omentum.

Lymph vessels and lymph nodes. The thoracic duct is the largest single lymph vessel in the body in both neonates and adults. It is about 10–11 cm long in the neonate. The right lymphatic duct that drains lymph from the right side of the head and neck is only 2–3 cm long and surrounded by lymph nodes. The total amount of lymphoid tissue in the form of lymph nodes is considerable in the neonate. Generally lymphoid tissues increase in amount during childhood because of the growth of nodes already present in the neonate. The pharyngeal tonsil (adenoid) is formed shortly before birth by infiltration of the pharyngeal bursa with masses of lymphoid cells. Definitive follicles with germinal centres are formed during the first postnatal year, and the pharyngeal tonsil reaches its maximal development at 6 years; thereafter involution is completed by puberty. The paired palatine tonsils are situated slightly higher in the tonsillar fossae in the neonate; each descends in position during the second and third postnatal year; definitive lymph nodules appear after birth. The palatine tonsils may begin to atrophy from the fifth year and involution is often complete by puberty.

ENDOCRINE GLANDS

Of the neonatal endocrine glands, the pancreas has been described under the gastrointestinal tract and the gonads under reproductive organs.

Thyroid gland (4.5). Relatively large in the neonate, it has a long narrow isthmus connecting lobes which do not yet contact the upper part of the trachea. The gland attains half the adult size by 2 years postnatally. Colloid is present in the gland from 3 months gestation and thyroxin by 4.5 months gestation.

Parathyroid glands. These are variable in size and position as in the adult. They double in size between birth and puberty. Parathyroid hormone (PTH) is produced from the 12th week of development.

Pituitary gland (hypophysis). About one-sixth the weight of the adult gland, it increases in weight to become about one-half the weight of the adult gland at 7 years, attaining adult weight at puberty. Throughout postnatal life the gland appears larger in females, in both size and weight.

EVALUATION OF THE NEONATE

The general condition of the neonate is evaluated as quickly as possible after delivery, traditionally using a grading of five clinical features devised by Virginia Apgar (1953). The five clinical features are (see 4.20):

heart rate
respiration
muscle tone
response to pharyngeal catheter
colour of trunk.

These are each given a score from 0–2 at 1 minute and 5 minutes after delivery; evaluation is repeated until the infant's condition stabilizes. Total scores of 0–3 indicate severe neonatal distress, 4–6 indicate moderate difficulty in adjusting to extrauterine life, and scores of 7–10 indicate little difficulty in adjustment. Whereas the Apgar score alone is a poor index of asphyxia, and resuscitation may be indicated regardless of a high score, a low Apgar score invariably indicates some sort of problem. Generally the Apgar score is used alongside a narrative description of the baby at birth. The improvement in the Apgar score from 0 to 20 minutes after delivery has become an internationally understood and accepted shorthand for describing the success or otherwise of the resuscitative effort; it provides valuable information for medical practitioners examining the baby during the first years of life (Roberton 1992).

Heart rate	Absent	Slow (less than 100 beats/min)	Greater than 100 beats/min
Respiratory effort	Absent	Slow or irregular	Good; crying lustily
Muscle tone	Limp	Some flexion of extremities	Active motion; well flexed
Response to pharyngeal catheter	No response	Grimace	Cough or sneeze; vigorous cry
Colour of trunk	Blue or pale	Body pink, extremities blue	Completely pink

4.20 The factors which are evaluated at birth in the Apgar scoring system. Each factor is scored from 0–2 giving a maximal score of 10. Evaluations are made at 1 minute and 5 minutes after delivery and repeated until the infant's condition is stable.

It is estimated that 1–2% of all newborn infants in the United Kingdom receive intensive care following birth. Many of these babies are born prematurely and some require cardiorespiratory and nutritional support for one to several weeks, or even months, until functional maturity of their organ systems has occurred. Others are mature at birth but the transition to extrauterine life has been complicated by conditions such as birth asphyxia, sepsis or hypoxia, often leading to persistent pulmonary hypertension. A small number of babies require intensive care because anatomical abnormalities have occurred during their in-utero development; examples of such conditions include congenital abnormalities of the heart, obstruction to the digestive system and herniation of the abdominal contents into the chest as a consequence of congenital diaphragmatic hernia. While many of these conditions can only be corrected by operative procedures, the babies will usually require intensive care before and after their surgery.

In order to provide effective intensive care, catheterization of a central vein for pressure monitoring, placement of a 'long-line' into, or near, the heart for intravenous feeding and insertion of an indwelling catheter into an artery for blood gas and arterial pressure monitoring are often required. For other infants, samples of cerebrospinal fluid, blood or urine are required to determine whether infection is present. Some of the more commonly performed procedures which are required in the newborn period are described below, with particular reference to the anatomical landmarks which are referred to to ensure safe and accurate localization.

Endotracheal intubation

The insertion of an endotracheal tube (ETT) is a procedure which is commonly performed for resuscitation of the

Birth weight (kg)	Nose to mid-trachea (cm)	Lips to mid-trachea (cm)
0.5	—	6.2
0.75	—	6.5
1.0	8	6.8
1.5	9	7.3
2.0	10	7.9
2.5	11	8.5
3.0	12	9.1
3.5	13	9.7

*Hodson & Truog 1987

Structure	Vertebral level
Vocal cords	C1–2
Thoracic inlet	T1
Carina	T3–4, or T4

*Blayney & Logan 1994

newborn at birth and subsequently to enable artificial ventilation. The ETT is introduced into either the nose or the mouth and guided through the vocal cords with the help of a laryngoscope. The tip of the ETT should be in the mid-trachea, well above the carina.

The required length of the tube can be estimated according to birth weight, as in Table 4.1, or, in an emergency, by measuring the distance from the tragus of the ear to the tip of the chin; the distance from the lips to the mid-trachea gives approximately the same measurement. Alternatively, a commonly used formula for the estimation of 'tip to lip' tube length is the '1-2-3 = 7-8-9 guideline'. This is based on the observation that, for a baby weighing 1 kg at birth, the distance from the lip to midtrachea is 7 cm; for a 2 kg baby it is 8 cm and for a 3 kg baby it is 9 cm (Tochen 1979). For nasotracheal tubes the formula takes into account the nasopharyngeal length needed and becomes '1-2-3 = 8-10-12'. These figure are also achieved by using the 7-8-9 figures plus the birth weight in kilograms (Kohelet et al 1982).

Confirmation of correct positioning of the ETT is obtained radiologically, either from a chest X-ray or, in order to minimize radiation exposure of the baby, from a 'coned view' of the trachea. The anatomical reference points used for the X-ray to assess the position of the ETT are the clavicles, the bodies of the vertebrae and the carina (although the latter is not always visible on X-ray). In the past it has been advised that the ETT tip should be placed just below the clavicles, at the level of the first rib (Fletcher et al 1983) or 1–2 cm above the carina (Carolene 1991). It has recently been suggested that, as positioning of the clavicles can vary according to angulation and placement of the baby and the carina cannot always be identified, the body of the first thoracic vertebra (T1) would be a more stable reference point as the target for the ETT tip (Blayney & Logan 1994). The length of the trachea in the neonate can be as short as 3.1 cm in premature infants (Coldiron 1968) and the distance from T1 to the carina ranges from 1.4 cm in babies weighing 500–1000 g to 1.8 cm in those weighing 3001–3500 g (Blayney & Logan 1994). Relevant anatomical reference points are given in Table 4.2.

Umbilical arterial catheterization

Insertion of an umbilical catheter is undertaken to provide direct access to the arterial circulation. This enables arterial blood to be withdrawn repeatedly for measurement of oxygen and carbon dioxide partial pressures, pH, base excess and many other parameters of blood biochemistry and haematology; the in-dwelling catheter also provides a facility for the continuous measurement of arterial blood pressure.

The catheter is inserted directly into either the cut end or the side of one of the two umbilical arteries in the umbilical cord stump which remains attached to the baby following transection of the umbilical cord at the time of delivery. The catheter tip is then advanced along the length of the umbilical artery, through the internal iliac artery, into the common iliac artery and from there into the aorta. In order to keep the catheter patent a small volume of fluid is infused continuously through it. It is important that the tip of the catheter should be located well away from arteries branching from the aorta, to avoid potentially harmful perfusion of these arteries with the catheter fluid. Thus umbilical arterial catheter tips are placed in the descending aorta either in a 'high' position, above the coeliac artery but well below the ductus arteriosus, or in a 'low' position, below the renal and inferior mesenteric arteries but above the point where the aorta bifurcates into the two common iliac arteries. The length of catheter to be inserted can be estimated from charts relating the required catheter length to external body measurements (Dunn 1966; Rosenfeld et al 1980), or from birth weight (Shukla & Ferrara 1986). Positioning of the catheter is assessed by means of abdominal and/or chest X-rays: a 'high' catheter tip should be located in the descending aorta somewhere between the levels of the sixth and ninth thoracic vertebrae (T6–T9), while a 'low' catheter tip should be at a level between the third and fourth lumbar vertebrae (L3–L4). Relevant anatomical reference points are given in Table 4.3.

Peripheral arterial puncture

It is common practice to insert a small-bore cannula into a peripheral artery in neonates receiving intensive care when either the umbilical artery is not accessible or there are clinical reasons to avoid cannulation of the umbilical vessels. Transillumination can be used to provide an outline of the artery to be cannulated (see below) (Pearse 1978). The peripheral arteries which are most commonly used are the radial artery, just above the anterior surface of the wrist, and the posterior tibial artery, posterior to the medial malleolus. The proximity of the ulnar nerve to the ulnar artery increases the risk of nerve damage associated with arterial cannulation of the ulnar artery, and the relatively poor collateral circulation associated with the dorsalis pedis artery means that this artery is used only as a last resort. The brachial artery at the antecubital fossa also has a poor collateral circulation and the median nerve is in close proximity; it is generally considered, therefore, that cannulation of this artery is not justified.

Confirmation that an adequate col-

Table 4.3 Key anatomical reference points for umbilical arterial catheterization

Structure	Vertebral level
Ductus arteriosus	T4–5
Coeliac artery	T12
Superior mesenteric artery	T12–L1
Renal artery	L1
Inferior mesenteric artery	L3
Aortic bifurcation	L4–5

Table 4.4 Key anatomical reference points relevant to lumbar puncture

Structure	Vertebral level
End of conus medullaris	L2
Iliac crests	L3–4
End of subarachnoid space	S1–2

lateral circulation is present when cannulating the radial artery can be obtained by performing *Allen's test*, in which both the radial and ulnar arteries are compressed at the wrist following exsanguination of the hand and forearm; release of pressure on the ulnar artery while maintaining occlusion of the radial artery should result in reperfusion of the hand and lower forearm if an adequate collateral ulnar arterial supply is present. Alternatively, intact arterial flow can usually be confirmed, particularly in the preterm infant, by direct visualization of the arteries using transillumination. A cold light source is placed on the posterior aspect of the lower forearm and the shadow of the pulsating arteries can be seen on the anterior surface of the forearm.

Umbilical vein catheterization

The umbilical vein is catheterized to enable exchange and transfusion of blood, for central venous pressure measurement and, usually in an emergency, for vascular access. The catheter is inserted into the cut end of the umbilical vein and is advanced along the length of the vein, through the ductus venosus and into the inferior vena cava, the tip being placed between the ductus venosus and the right atrium. Positioning of the catheter tip is confirmed radiologically and it should be located just above the diaphragm at a point which is level with the ninth or tenth thoracic vertebrae (T9–T10). As with umbilical arterial catheters, estimation of the required catheter length can be determined from standard charts (Dunn 1966).

Percutaneous central venous catheterization

Small-bore catheters can be fed into large central veins or into the right atrium via needles or catheters inserted in the peripheral veins. Typically, the median cubital or basilic veins are used in the upper limb and the great saphenous at the medial malleolus in the lower limb. The tip of the catheter is sited at the entrance to the right atrium. The required catheter length is assessed from direct measurement of the distance between the point of surface entry in the limb to the right atrium, estimated at midsternal level.

Lumbar puncture

Cerebrospinal fluid (CSF), obtained by lumbar puncture, is often needed to determine whether meningitis is present. CSF surrounds both the spinal cord and the cauda equina; when bacterial meningitis occurs an increased inflammatory cell influx can be demonstrated by microscopical examination of CSF and pathogenic bacteria can be identified by culture and microscopy.

During gestation the relationship between the conus medullaris and the vertebral column changes such that the conus medullaris gradually ascends to lie at higher vertebral levels. By 19 weeks of gestation the conus is adjacent to the fourth lumbar vertebra (L4), and by full term (40 weeks) it is at the level of the second lumbar vertebra (L2). By 2 months postnatally the conus medullaris has usually reached its permanent position at the level of the body of the first lumbar vertebra (L1) (Barson 1970). In performing a lumbar puncture it is important to enter the spinal canal below the level of the termination of the spinal cord, the tip of the conus medullaris. While this is usually at or above the level of the second lumbar vertebra (L2), in some individuals the cord may, rarely, extend as low as L3 and it is advisable, therefore, for the needle to enter the spinal canal below this level.

A lumbar puncture is performed by placing the baby in a position, either lying or 'sitting', which gives maximum convex curvature to the lumbar spine. A needle with trochar is inserted into the back between the spines of the third and fourth vertebrae and into the subarachnoid space below the level of the conus medullaris. The space between L3 and L4 is approximately level with the iliac crests and it is usual to insert the needle and trochar into the intervertebral space immediately above or below the iliac crests. The needle and trochar pass through the interspinous ligament, the ligamentum flavum, the dura mater and the arachnoid mater (see Table 4.4).

Suprapubic aspiration of the bladder

In infants under the age of two years, and particularly in neonates, urine is often collected, either as part of a general sepsis screen, when infection is suspected but neither certain nor localized, or when a specific urinary infection is suspected. In either case, there may be some urgency in initiating treatment with antibiotics and the urine must be collected before such treatment is started in order to avoid a partially treated specimen giving misleading results.

In young infants a large portion of the bladder, when it contains urine, is located above the level of the symphysis pubis, in the lower abdomen rather than in the pelvis. It is possible, therefore, to obtain urine by inserting a needle, connected to a syringe, into the bladder through the abdominal wall about 2 cm above the symphysis pubis and aspirating the contents into the sterile syringe (Nelson & Peters 1965). Since urine is obtained directly from the bladder it cannot have been contaminated by organisms around the perineum and anus, as it might be if the urine is passed into a bag or container; any growth on culture, therefore, is regarded as significant and indicative of urinary infection.

The success rate of the procedure is variable and depends upon the bladder being full. Recently, a much higher success rate has been reported by using an ultrasound scanner to locate the bladder and confirm that it contains urine prior to the insertion of the needle (Buys et al 1994).

Growth is a term widely used in everyday conversation and applied to both living and inanimate objects; commonly it implies an increase in mass or size. The section which follows is concerned with this general concept as it applies to the growth of cells, tissues and organs constituting a whole animal. Within this context, and indeed in others, it becomes evident that the simple definition 'increase in mass and size' is not entirely satisfactory; it becomes necessary to distinguish between different types of growth to appreciate the complex nature of the process and the exquisite control mechanisms involved.

TYPES OF GROWTH

At the cellular level distinctions can be made between protein and DNA synthesis leading to an increase in cell number by mitotic division, *cellular hyperplasia*, and synthesis of protein and cellular material without mitotic division leading to an increase in cell size, *cellular hypertrophy*. Also at this level growth may be described with reference to the amount of extracellular matrix produced by the cells (this is termed *accretionary growth*) or by the position in which cells and extracellular matrix are added, i.e. either within a tissue as in *intestinal growth* or to its surface, as in *appositional growth*.

Cellular hyperplasia

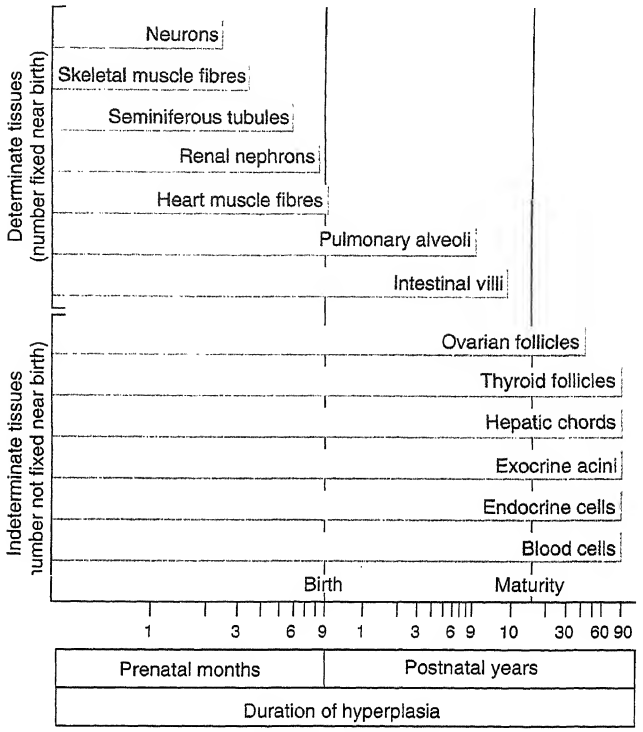
Within the normal life cycle *hyperplasia*, or *multiplicative growth*, is seen during the developmental stages of embryogenesis, organogenesis and gestational growth, and also in infancy and childhood. Generally, hyperplastic growth decreases as the individual approaches sexual maturity; however, each cell lineage normally remains in multiplicative growth for differing time periods such that whereas some cells, for example neurons, complete their mitotic proliferative phase in utero, other cells, for example type I alveolar epithelial cells, continue to divide during childhood, while still other cells, for example stem cells for blood production, divide continuously for the lifetime of the individual (see **4.21**).

Cell division is controlled at two main levels, extrinsic and intrinsic; these levels correlate to the distance effector substances travel to exert their effect. Extrinsic control of cell division depends on factors from other tissues (a hormonal effect), whereas intrinsic control depends on factors produced locally by the cells themselves (a paracrine effect).

Cellular hypertrophy

Hypertrophic or *auxetic growth* involves an increase in the size of the specific individual cells characterizing a tissue without their division. It is usually seen in cells which can no longer undergo mitosis and therefore is mainly a feature of postnatal life. It is particularly prominent in certain invertebrate tissues such as the salivary glands of Diptera, but is also well shown by some mammalian tissues. For example, there is a vast postnatal increase of both surface area and cytoplasmic volume in many neurons and glial cells; the growing striated muscle fibre, the oöcyte, the myelinating Schwann cells, and the smooth muscle cells of the pregnant uterus furnish further obvious examples. The majority of other tissues, however, show some hypertrophic growth but of limited degree, while conversely, in some sites, continued multiplicative growth is accompanied by a **reduction** in cell volume (e.g. granule cells of the cerebellar cortex, and small lymphocytes in lymphoid tissue).

It is widely held that the general nucleocytoplasmic ratio to which most of the body's cells roughly approximate reflects the fixed quantity of DNA in their diploid nuclei which, in turn, imposes a rate limitation on the replacement of cytoplasmic proteins (each of which has a characteristic turnover rate). Thus, with continuing auxetic growth of a cell, its cytoplasmic volume eventually reaches a point beyond which the structural genes cannot effectively replace the protein which is undergoing continual degradation. In some cases, growth ceases at this point, or nuclear replication with cell division occurs. The cases of hypertrophic growth cited above, however, often proceed far beyond the usual ratio of cytoplasmic volume to nuclear material and, in these, various methods of providing auxiliary nuclear support have emerged. The large dipteran salivary gland cells develop 'giant' polytene chromosomes containing some multiple of the diploid DNA content. The striated muscle fibre and other 'giant' cells such as megakaryocytes are, of course, multinucleate syncytia. Finally, the enlarging oöcyte and neuron (possessing but a single haploid and a single diploid nucleus, respectively) have their surfaces clothed by numerous satellite cells (follicular or glial cells). Such satellites probably provide auxiliary metabolic and nuclear support for the enlarged central cell, i.e. the two are functionally interlocked as a *cytophysiological unit*.



4.21 The duration of multiplicative growth for various human tissues (after Gilbert 1992).

Hypertrophic growth can be induced; for example, muscle fibres enlarge when exercised and adipose cells enlarge with fat deposition in obesity.

Accretionary growth

Accretionary growth denotes an increase in the amount of extracellular matrix between tissue cells rather than either an increase in cell number or of cell size. Bone and cartilage are the most commonly cited examples; other less obvious examples are the other fibrous connective tissues, tendons, joint capsules, aponeuroses, fasciae, and the cornea.

Appositional growth

Appositional growth is a specific type of growth where new generations of cells and extracellular matrix are added to the surface of the tissue by the repeated division of the cells of a cambial layer which surrounds the tissue, for example periosteum and perichondrium.

Interstitial growth

Interstitial growth is seen where multiplicative and sometimes accretionary growth continues throughout the thickness of a tissue mass and it grows as a whole expanding from within.

Meristematic growth

Meristematic growth describes growth from a tip which contains populations of dividing cells. As division occurs the tip moves distally leaving populations of cells from its early divisions. An example of meristematic growth is seen in the limb buds where the progress zone produces first cells of the shoulder, then is moved distally to produce populations of the arm, and so on.

Compensatory growth

Tissue and organ growth is normally under some sort of control: a balance is achieved between loss through 'wear and tear' and the maintenance of functional tissue integrity. Large-scale loss can be compensated for either through regeneration of the tissue itself, as in the liver, or by compensatory growth elsewhere, for example following the loss of one kidney. Compensatory growth, however, appears to be strictly regulated; regenerating liver, for instance, more or less regains its original size, at which point growth ceases.

Integration of types of growth

In the later gestational months and the postnatal period all the types of growth are welded together in various patterns, with differential growth rates and directions in different parts of the system. For example, in the developing limb whereas the production of the mesenchymal populations may be an example of meristematic growth, the overlying ectoderm, in contrast, grows interstitially. Generally the differential growth patterns with either random or preferentially polarized directions of mitotic division, together with alterations in cell size, shape and surface consistency, are central features of embryonic development and are responsible for the moulding of tissues into specific shapes whether solid masses, hollow balls, tubes, sheets and so forth. Equally important in some regions, however, is a process of tissue regression, with degeneration, cell death and tissue removal.

PATTERNS OF GROWTH

When describing growth patterns of a whole body two types of growth can be considered, *isometric growth* and *allometric growth.*

Isometric growth

True isometric growth would imply a progressive proportional increase of all organs and systems with time. Clearly isometry does not occur in developing embryos where differential rates of growth obtain, a process termed allometric growth.

Allometric growth

Allometric growth describes the differences in the relative rates of growth between one part of the body and another. It is most clearly seen in the changes in body proportion between fetuses, neonates, children and adults. Between 6 and 7 weeks after fertilization the head is nearly one-half of the total embryonic length. Subsequently during gestation the head grows proportionally more slowly so that at birth it is one-quarter of the whole length. During childhood this pattern of growth continues with lengthening of the torso and limbs until, in adults, the head is one-eighth the length (4.22).

Allometric growth can be considered to be responsible for the variation of the vertebrate body plan, especially in, for example, skull development in mammals. It has been suggested that a basic pattern for the base of the skull is specified by the basal layer of the neural tube (see p. 274). The initial stimulus to chondrogenesis is provided by the neurepithelial cells resulting in the arrest of migration of underlying migrating mesenchymal cells. The pattern of arrest forms the template for the base of the skull. In mammals there is some modification of the skull prior to birth but generally the mammalian skull is globular, assisting passage along the birth canal. After birth the specific skull shape for the species develops by allometric growth, resulting in either the flat, neotenous human skull, the more prognathous skulls of lower primates or the relatively extreme elongation of the skulls in horses or anteaters.

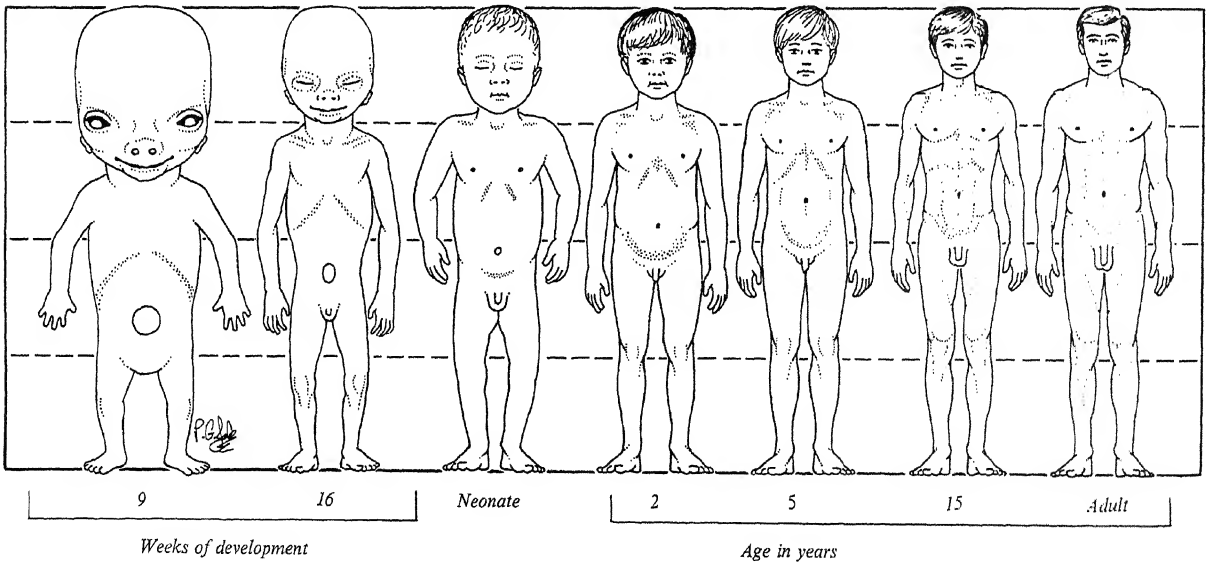
GROWTH HORMONES AND GROWTH FACTORS

Growth during the embryonic, fetal and postnatal period is controlled by a variety of processes which are as yet not understood. Postnatal growth is profoundly affected by the circulating levels of growth hormone (GH or somatotropin); growth-hormone releasing hormone (GHRH) and somatostatin; however, these hormones have not been shown to control fetal growth.

Growth hormones (GH)

Growth hormone can be detected in fetal serum by 100 days gestation (Kaplan et al 1972), the level increasing in concentration up to 30 weeks but falling in the last trimester, although the level at birth is still elevated compared to that of the mother. The level of growth hormone remains fairly constant from birth until the end of the first postnatal year.

The role of growth hormone in the fetus is unclear. Because anencephalic babies and those with genetically determined growth hormone deficiencies attain lengths within normal limits it has



4.22 Allometric growth in humans. The head is very large in proportion to the rest of the body during the embryonic period. After this time the head grows more slowly than the torso and limbs and by adulthood the head is only one-eighth of the body length.

been assumed that fetal growth is independent of pituitary growth hormone, a view noted as hazardous by Hindmarsh and Brook (1988).

However, the role of growth hormone in the postnatal period has been the subject of extensive study. It is clear from epidemiological studies that growth hormone is necessary after the first 2–3 months, if not before. All tissues respond to growth hormone producing a proportional body growth which slows after puberty when secretion of the hormone decreases. The effects of growth hormone are seen particularly on the epiphyseal growth plates of the long bones. Continued secretion of growth hormone will result in giantism and lack of the hormone produces proportional dwarfism. In cases of acromegaly where growth hormone is abnormally secreted (after the epiphyseal growth plates have fused), the presenting symptoms develop over many years, with enlargement of the heart and liver, thickening of the bones especially the maxilla and mandible, and thickening of the skin. Thus, in this case, all the cells and tissues which are normally responsive to growth hormone continue proliferating.

A series of complicated experiments have elucidated the specific effects of growth hormone. The gene for growth hormone was isolated in the rat and combined with a mouse gene which regulates serum zinc levels (mouse metallothionein I) to act as a promoter. The combined gene was injected into mouse pronuclei shortly after fertilization, resulting in mice with both the rat growth hormone gene and the mouse metallothionein I gene within their chromosomes. Some of the transgenic mice were then fed a diet which included zinc supplements which switched on the rat growth hormone gene inducing synthesis of rat growth hormone from the liver (the normal site of metallothionein). The transgenic mice with the zinc supplement became up to 80% larger than their littermates, with all of their organs in proportion (Palmiter et al 1982). These elegant experiments demonstrate that growth hormone controls the co-ordinated regulation of growth.

Somatomedins/insulin-like growth factors

At the cellular level growth hormone acts by stimulating somatomedin synthesis by the liver. Somatomedins are a family of insulin-like growth factors (see p. 56) including insulin-like growth factor I (IGF-I or somatomedin C) and insulin-like growth factor II (IGF-II or somatomedin A).

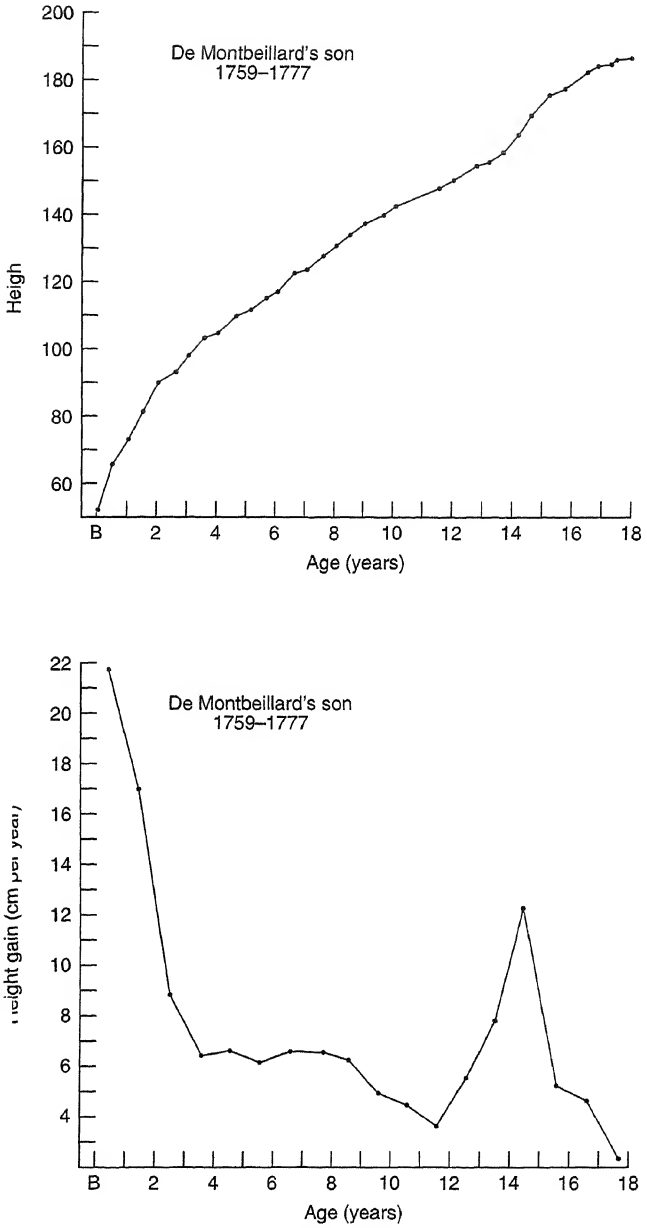
It has been noted that in the human embryo IGF-I levels are low and administration of growth hormone does not affect growth at this time (Hall & Sara 1983). IGF-II levels on the other hand are elevated in the fetus and their levels are not influenced by growth hormone. It has thus been suggested that the regulation of growth in the fetus is mainly regulated by IGF-II, which, in turn, may be controlled by placental lactogen (Engstrom & Heath 1988). Due to its widespread expression in the embryo and fetus IGF-II has been proposed to be the major paracrine growth factor in vivo and a major determinant of fetal growth.

There is a positive correlation between birth weight and plasma concentrations of IGFs at delivery, with decreased levels of IGFs observed in small for gestational age children. During the growth spurt of adolescence the levels of GH, IGF-I and IGF-II are increased. In pygmies the level of both GH and IGF-I is normal; however, at puberty IGF-I secretion falls to one-third compared to other adolescents, suggesting that IGF-I is necessary for the normal pubertal growth spurt (Merimee et al 1987).

Other growth factors

Various families of growth factors are discussed in the Introduction section (see p. 56) and elsewhere (see p. 112). In brief, *platelet-derived growth factor* (*PDGF*) stimulates division of fibroblasts, smooth muscle and glioblasts; *epidermal growth factor* (*EGF*) promotes division in, inter alia, epidermis, mammary gland epithelium and skeletal muscle.

Interestingly, a wide range of growth factors are secreted in breast milk. EGF is the major growth factor in human milk, unlike cow's milk which contains no EGF. Insulin is detected in low concentrations in human milk and IGF-I concentrations are 10% of those in normal human serum (Read 1988). The concentrations of these growth factors change during lactation, being maximal in day 1 colostrum and declining during the first week to reach a plateau. Despite this fall human milk still contains EGF and insulin at 10% of the concentrations in colostrum. Read et al (1984) have suggested that the total growth factor delivery to the baby remains nearly constant throughout lactation. As endogenous production of EGF is undetectable in the neonatal period, human milk may provide the baby's only source. However, as neonates maintained entirely on artificial formulae develop at apparently normal rates it seems unlikely that growth factors in milk are essential requirements for normal growth; Read (1988) suggests that growth factors may exist in milk as an emergency measure to improve the efficiency of neonatal growth under conditions of poor nutrition or inadequate development.

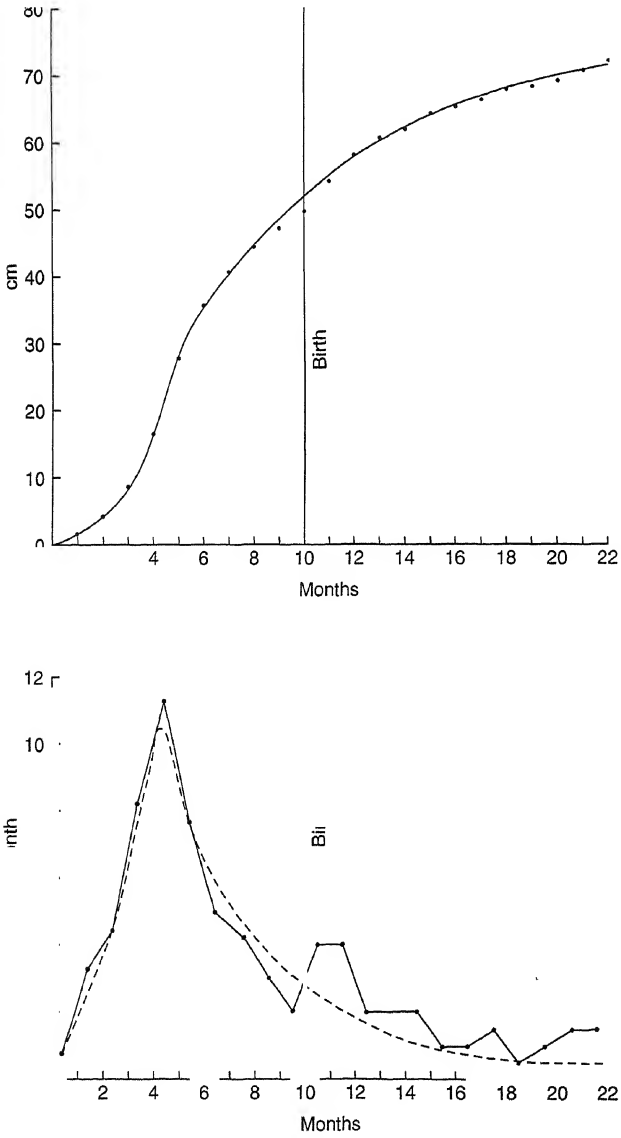


4.23 Graphs showing a longitudinal study of growth. The height of de Montbeillard's son (1759–77) from birth to 18 years is shown in the upper chart. The lower chart shows a velocity curve, plotting increments in height from year to year (from Harrison et al 1964).

GROWTH RATES

The rate of prenatal and postnatal growth can be indicated by

increments in body length or weight which when plotted form a *growth curve*. Growth curves can be plotted for individuals if accurate measurements are taken, preferably by the same person, for the entire period of growth, a *longitudinal study*. An alternate method is to collect a series of averages for each year of age obtained from different individuals; this is a *cross-sectional study*. Cross-sectional studies are valuable for the construction of standards for height and weight attained by healthy children at specific ages, and can establish percentile limits of normal growth; however, they cannot reveal individual differences in the rate of growth or in the timing of particular phases of growth. Longitudinal studies are thus of great value but laborious and time consuming to those undertaking them. The data from longitudinal and cross-sectional studies can also be used to plot the increments in height or weight from one age to the next; this forms a *velocity curve*: it reflects a child's state at any particular time much better than the growth curve in which each point is dependent on the preceding one. The oldest published longitudinal study, still of great value today, was made by Count Philibert de Montbeillard upon his son (4.23). It shows that the velocity of growth in height decreases from birth onwards with a marked acceleration of growth from 13 to 15, the *adolescent growth spurt* (see below).



4.24 Graphs of cross-sectional data showing growth in length in the prenatal and early postnatal period, and the corresponding velocity curve for this period (from Harrison et al 1964).

Cross-sectional data have provided comparison of prenatal and postnatal growth, and childhood growth charts are used to predict normal childhood development. The velocity curve for the prenatal and postnatal period (4.24) shows that the peak velocity for length is reached at about 4 months (note that these prenatal charts use the obstetric measurements of gestational time where fetal age is estimated from the last menstrual period, 2 weeks prior to fertilization). Growth in weight reaches its peak velocity usually after birth.

Growth has always been regarded as a regular process. Tanner (in Harrison et al 1964) stated that growth does not proceed in fits and starts, noting that the more carefully the measurements are taken, the more regular is the succession of points on a growth curve. However, a longitudinal study of growth measured weekly, semi-weekly, and daily (Lampl et al 1992) demonstrated growth in length and head circumference occurring by saltatory increments with a mean amplitude of 1.01 cm for length. Growth saltations were not periodic but episodic. This study proposes that human growth in length, during the first 2 postnatal years, occurs during intervals of less than 24 hours that punctuate a background of stasis. They suggest that stasis may be part of the normal temporal structure of growth and development. A cautionary note is provided by Wales & Gibson (1994) who, while concurring that growth in height is not a steady process but one made up of intermittent episodes of growth, add that, because of the range of factors which may affect growth, the problem of accurate measurement and the type of mathematical model used to explain growth, predictions of long-term growth from short-term observations, either of one bone or of the whole body, should not be attempted.

Effect of maternal environment

The rate of growth of fetuses slows from about 36 to 40 weeks due to the limiting influence of the maternal uterus. Birth weight thus reflects the maternal environment more than the genotype of the child. This slowing of the growth rate enables a genetically larger child developing within a small mother to be delivered successfully, after which the growth rate of the neonate picks up and in weight reaches a peak some 2 months postnatally.

This limit of prenatal growth imposed by the maternal uterus was demonstrated experimentally many years ago by the crossing of large Shire horses and Shetland ponies. A Shire mare crossed with a Shetland produces a foal of similar size to a pure-bred Shire foal, whereas a Shetland mare crossed with a Shire horse produces a foal only a third as large, similar in size to a pure-bred Shetland foal (Walton & Hammond 1938).

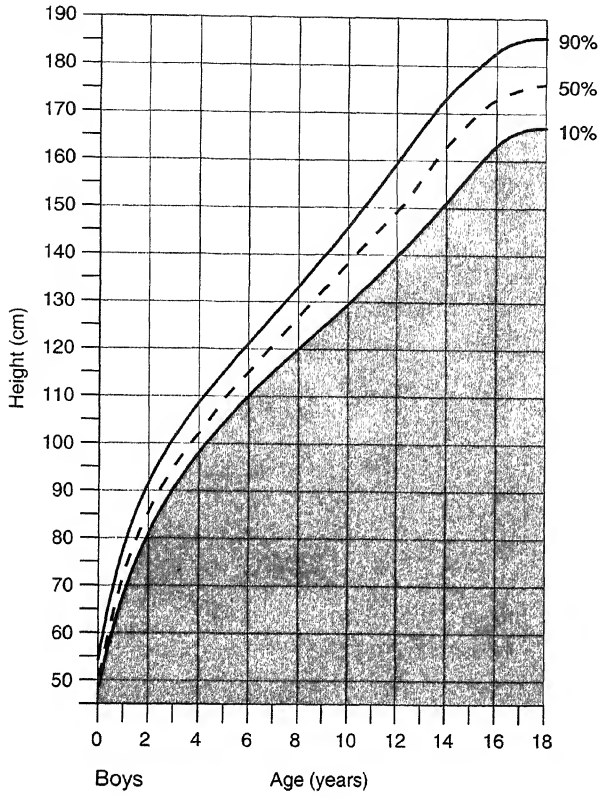
The predominant influence of the mother on the size at birth is steadily eroded as the infant's genotype expresses itself and by adult life the offspring bears no greater resemblance to the mother than to the father. Thus in the horses, after weaning when the foals are under the same nutritional conditions, the Shetland/Shire crosses rapidly outgrow pure-bred Shetlands; however, they do not keep up with pure-bred Shires.

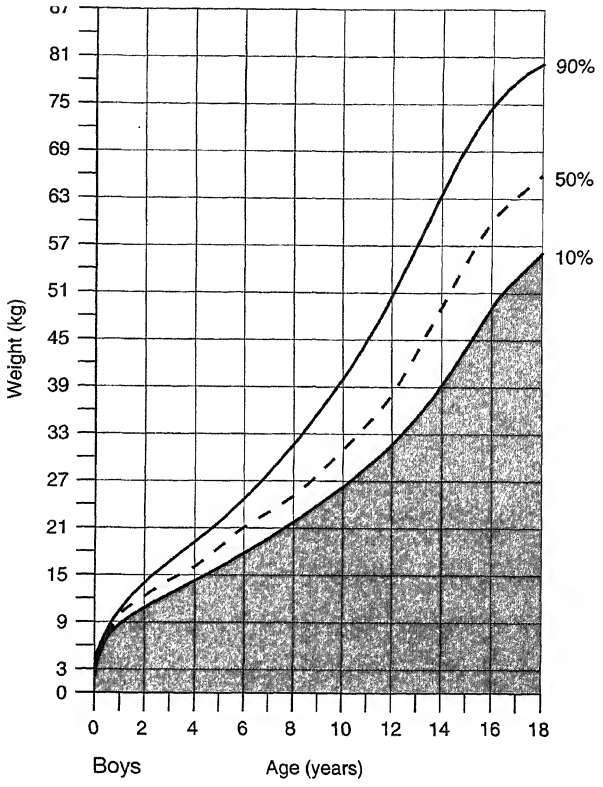
Standard growth charts

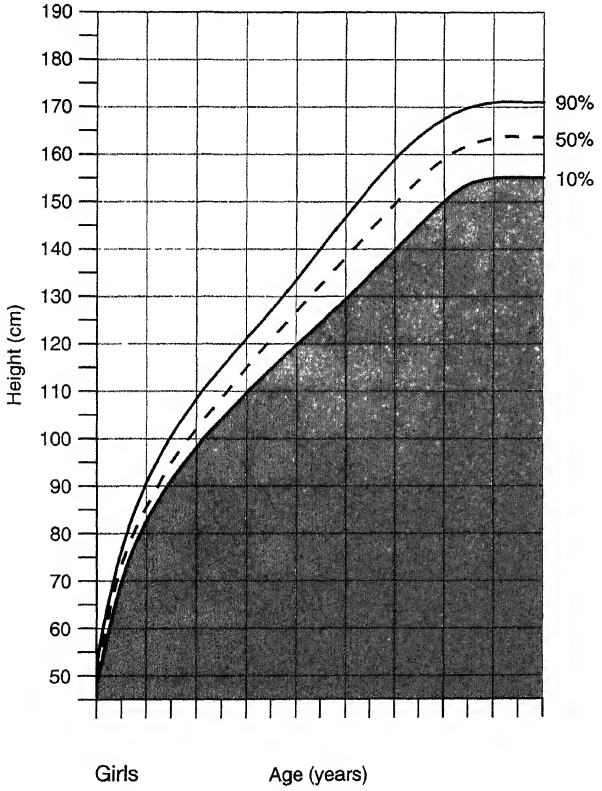
Charts of height and weight correlated to age are compiled from extensive cross-sectional growth studies. Such charts show the mean height or weight attained at each age, also termed the 50th centile, and also the centile lines for the 75th, 90th and 97th centiles as well as the 25th, 9th and 2nd centile. The data shown in 4.25 are derived from United Kingdom cross-sectional references. Any comparison of an individual growth curve with these data should also take into account the ethnicity, nutritional and family history of the individual.

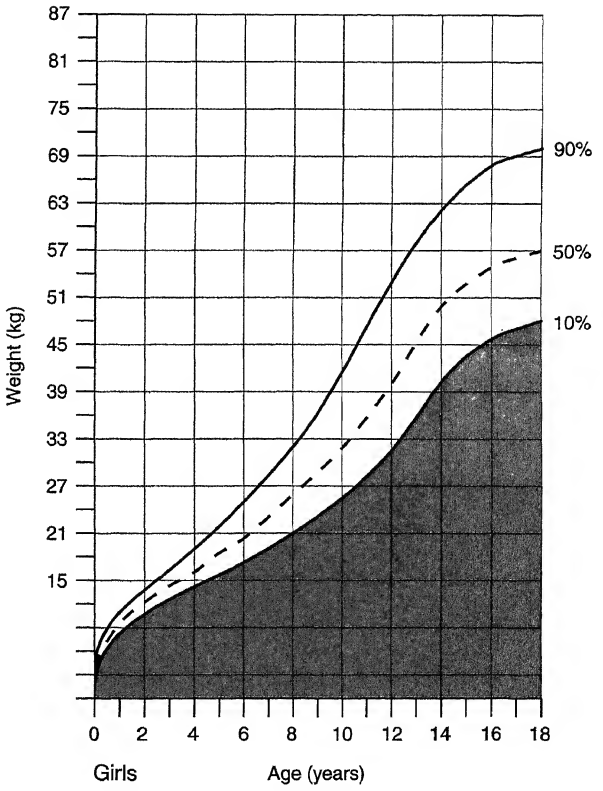
Adolescent growth spurt

From growth charts it can be seen that during the first year after birth body **length** increases from a neonatal range of 48–53 cm to about 75 cm, and in the second year by 12–13 cm. Thereafter 5–6 cm are added each year. In individual longitudinal growth curves an increase in the velocity of growth can be seen from 10.5–11 years in girls, and 12.5–13 years in boys. This rapid increase in growth is termed the *adolescent growth spurt* (4.25, 26). In both sexes this growth spurt lasts for 2–2.5 years. Girls gain about 16 cm in height during the spurt, with a peak velocity at 12 years of age; boys gain









4.25 Standard growth charts of boys and girls showing the 90th, 50th and 10th centiles. (Data from Child Growth Foundation 1994/1).

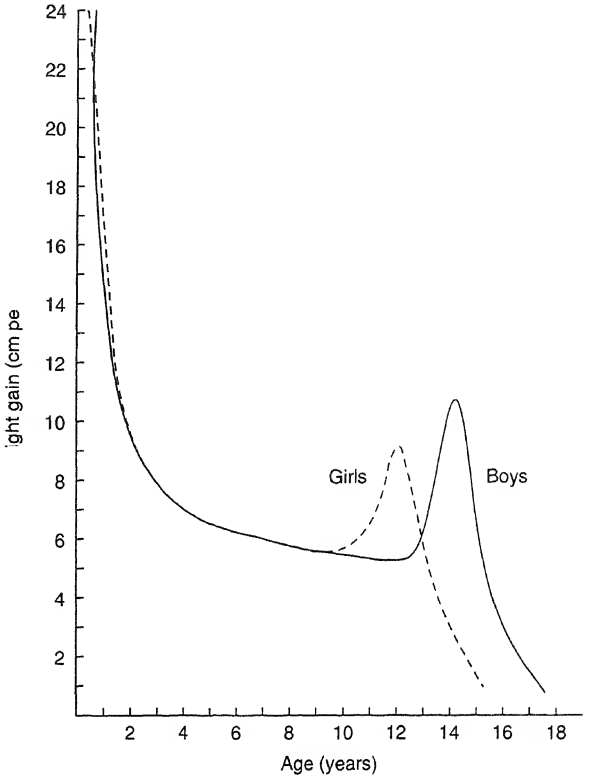
about 20 cm in height (mostly by growth of the trunk), with a peak velocity at 14 years of age during which they may be growing at the rate of 10 cm a year.

Humans seem to be the only species which has a long quiescent interval between the rapid growth immediately after birth and the adolescent growth spurt. It has been suggested that this time allows the brain to mature and learning to take place before individuals pass through puberty and become sexually active.

Growth in height continues at a slower rate after the adolescent growth spurt and noticeable growth is said to stop at about 18 years in females and 20 years in males (longitudinal studies have indicated that an average figure for this is 16.25 for girls and 17.75 for boys with a normal variation of ±2 years; Harrison et al 1964). After this time any increments, which occur because of appositional growth at the cranial and caudal ends of the vertebral bodies and intervening intervertebral symphyses (discs), are so small as to be difficult to measure; after middle age there is a loss of height.

The phenomenal growth rates of adolescence are seen particularly in increased height. **Weight** gain is more variable. At birth, weight reflects the maternal environment, the number of conceptuses, the sex of the baby, and the parity of the mother. Generally full-term female babies are lighter than full-term males, twins are lighter than singletons and later children tend to be heavier than the first-born. Although the birth weight seems to be independent of the mother's diet unless there has been severe malnutrition, mothers in a low socioeconomic group have smaller babies than those with a higher rating, and small mothers tend to have small babies (see above).

The birth weight is normally tripled by the end of the first year and quadrupled by the end of the second year. Thereafter weight increases by 2.25–2.75 kg annually until the adolescent growth spurt when boys may add 20 kg to their weight and girls 16 kg. The peak velocity for weight gain lags behind the peak velocity for height by about 3 months. Body weight does not reach adult values until some time after adult height is attained.



4.26 Typical individual velocity curves for height: English boys and girls (from Tanner et al 1966).

A very interesting relationship is now emerging between the nutritional status of the fetus in utero and patterns of pathology in late adult life. The routine assessment of weight and height of the neonate, and the re-evaluation of weight and height at 1 year of age was rigorously followed in the early years of this century in many counties in the United Kingdom. Many of these data, filed with the old birth records, remained untouched for more than 50 years, until recently when its rediscovery prompted follow up studies on as many of the original population documented as possible. Studies by Barker et al (1993a,b,c) noted the cause of death or survival health of 1586 men born in a maternity hospital in Sheffield during 1907–25, and of 5654 men born in Hertfordshire during 1911–30. Such longitudinal studies are of great value in correlating in utero status, which may be inferred by birth weight and weight at 1 year postnatally (when the peak velocity for growth in weight has occurred, see above), with childhood and adult lifestyles and with later pathology.

Generally these studies indicated that men with low birth weight and low weight at 1 year of age (on or below the 3rd centile on the standard growth chart, see 4.25) were almost three times more likely to die of coronary heart disease than those who attained average weight at birth and at 1 year. Examination of other populations of both sexes similarly indicated that low growth rates up to 1 year of age were associated with increased prevalence of known risk factors for cardiovascular disease, including altered blood pressure, plasma concentrations of glucose, insulin, fibrinogen, factor VII, and apolipoprotein B (Barker et al 1993a). These associations were seen in babies born small for gestational age rather than in those born prematurely; however, as well as this population of infants with intrauterine growth retardation, some babies of average weight also developed later cardiovascular pathology. This latter group were small at birth in relation to the size of their placenta, were thin at birth, or, although of average weight, were short in relation to head size and had below average weight gain during the first year.

Barker and colleagues have postulated that poor nutrition at critical stages of fetal life may permanently alter the normal developmental pattern of a range of organs and tissues, for example endocrine pancreas, liver and blood vessels, resulting in their pathological responses to certain conditions in later adult life. Such a relationship has been demonstrated experimentally in animal studies. Low birth weight in the guinea pig, caused by retardation of intrauterine growth, causes lifelong elevation of blood pressure (Persson & Jansson 1992). In the rat, a low protein diet can induce a high ratio of placental weight to birth weight. Such rats have reduced placental activity of 11-B hydroxy-steroid dehydrogenase, which may protect them from excessive maternal cortisol (the fetal blood pressure is partly regulated by cortisol), and have raised blood pressure 15 weeks after birth (Barker et al 1993b).

As different tissues and organs mature at different times in fetal life and infancy any long-term consequences of in utero

malnutrition would depend on its timing and duration. Different birth phenotypes have been correlated with different pathological sequelae; for example infants who are thin at birth, with a low ponderal index (weight/length^3), tend to develop a combination of insulin resistance, hypertension, non-insulin-dependent diabetes, and lipid disorders, whereas those who are short in relation to head size tend to develop hypertension and high plasma fibrinogen concentrations (Barker et al 1993c).

Thus it is suggested that alterations in the availability of nutrients to the fetus, at particular stages of pregnancy, cause adaptive responses by the fetus which ensures fetal coping, but lead on to pathology in adult life when different conditions operate. Examples of this are as follows:

- An increase in placental size occurs in pregnancy as an adaptive response to both high altitude and mild undernutrition during midpregnancy. The larger placenta may be more able to deliver the full nutritional requirements of the fetus; however, the perfusion of a larger placenta may produce changes in fetal blood flow, changes in placental enzymes (see above), and change the normal structure of the vessel wall or of its responses to circulating trophins, for example catecholamines or angiotensin II, which will continue into adult life. Undernutrition in later pregnancy would not produce the same sequelae and placental enlargement does not occur; however, fetal growth slows and fetal wasting may occur as oxygen, glucose and amino acids are redistributed to the placenta to maintain its function.

Maternal starvation lowers fetal insulin-like growth factor (IGF)-I concentrations which may, along with a general hypoglycaemia, impair the development of the β-cells of the pancreas; generally fetal undernutrition may induce insulin resistance in the tissues. The coexistence of both insulin resistance and impaired β-cell development in the fetus appears to be important in the pathogenesis of non-insulin-dependent diabetes. The risk of developing this type 2 diabetes is highest in those individuals with low weight at birth and at 1 year, who become obese as adults, thus challenging an already impaired glucose-insulin metabolism.

- Fetal IGF-I levels are also lower in infants who are short at birth as a result of a long period of maternal undernutrition. Such individuals have exaggerated responses to growth hormone-releasing factor (GHRF), which together with low IGF-I levels suggests a degree of growth hormone (GH) resistance. Barker et al (1993) suggest that in such individuals the normal development of their hepatic GH receptors may have been attenuated.

These studies suggest that undernutrition in pregnancy may cause fetal adaptations which permanently alter the structure and physiology of the body possibly leading to a variety of pathological conditions in adult life. The implications of these findings is that the nutritional status of pregnant women is of fundamental importance for the health of the next generation. Further studies which illuminate this hypothesis are awaited with interest.

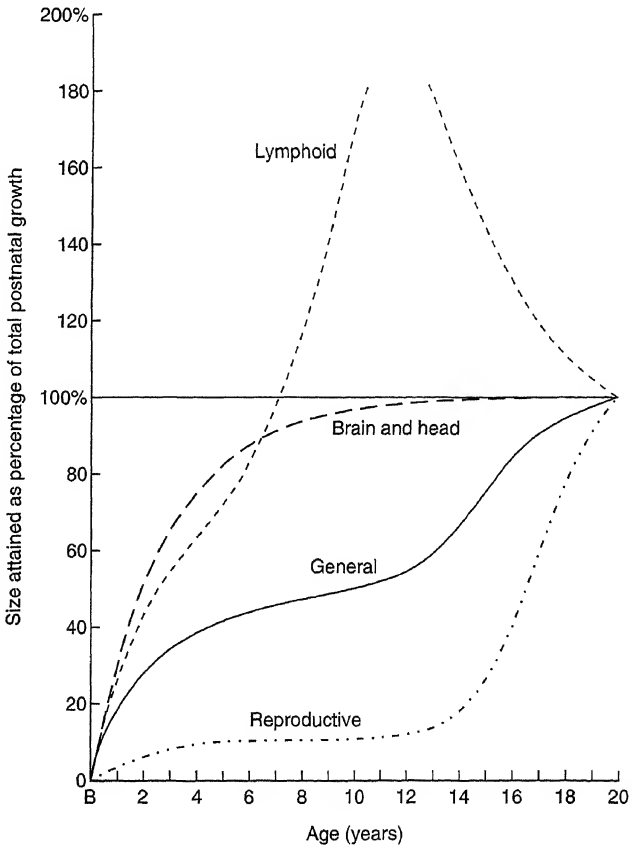
Growth rates of tissues and organs

Although skeletal and muscular tissues generally follow the growth curves given for the whole body, as do the dimensions of organs such as the liver, spleen and kidneys, other tissues have very different growth rates. The brain and skull, lymphoid tissues, reproductive organs and subcutaneous fat show differing growth rates during childhood and adolescence (4.27).

Head. This develops early and in response to the general craniocaudal progression of embryonic development, with the brain, skull, eyes and ears developing earlier than other parts of the body. After birth, the surrounding skull thickens with age and continues ossification towards the sutures; the face, however, is relatively underdeveloped and undergoes profound changes throughout childhood and at the adolescent spurt, resulting in the eruption of the deciduous and permanent teeth, the formation of the sinuses, and the elongation of the maxilla and mandible (4.28).

Limbs. It is worth noting at this point that although the bones and muscle of the limbs contribute to the growth spurt in height, there are some changes in relative proportions within this process. The male forearm is longer relative to the upper arm than the female forearm, a difference already established at birth which increases throughout the growing period. A similar difference is noted in the sex difference in relative lengths of the second and fourth fingers. The second finger is longer than the fourth more frequently in females than in males at birth. After birth, at all ages, the dimensions of the head are in advance of those of the trunk, and the trunk is advance of the limbs. However, the more distal parts of the limb are in advance of the more proximal parts; thus the foot is nearer adult status than the calf, which is in turn more advanced than the thigh. The time at which the hands and feet are large relative to the rest of the body coincides with the adolescent growth spurt; the foot ceases growth early before almost all other parts of the skeleton.

Lymphoid tissues. These include the thymus, tonsils, appendix and intestine and show an earlier growth curve compared to other tissues. They reach their maxima before adolescence and then, probably under the influence of the sex hormones, decline to adult values (4.27). The thymus is found in the superior and anterior mediastina in childhood. In the infant it weighs on average 13 g, reaching a maximum weight of about 35 g in girls at 12 years and



4.27 Growth curves of different tissues, regions of the body and systems. Note that the growth of lymphoid tissue, thymus, lymph nodes and intestinal lymph masses decreases after puberty (from Tanner 1962).